SACHS & FASMAN

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A TREATISE ON

DIAGNOSTIC METHODS

OF EXAMINATION

BY

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EDITOR'S PREFACE

The first edition of the English translation of Prof. Sahli's renowned book has met with a popularity scarcely equaled by that of the various German editions. It, therefore, seems unnecessary to comment at length upon the appearance of the second edition, which is as accurate and idiomatic a translation of the fifth German edition as I have been able to make.

The mistakes that crept into the first translation have been corrected and further editorial comments have been added. Several new diagrams and cuts have been inserted. The extensive alterations and complete revision of this latest German edition have, however, precluded the necessity for presenting to the English-speaking medical world more than the subject matter offered by the distinguished Swiss clinician.

Dr. C. G. L. Wolf, Professor of Chemistry in Cornell University Medical School, has edited the purely chemical portions of the text, and Dr. E. G. Zabriskie, Adjunct Professor of Neurology at the Postgraduate Medical School, has similarly edited the neurological section. Their editorial notes are designated by their initials. For their valuable assistance, and especially for that of my assistant, Dr. Wilson G. Wood, I wish to express my sincere appreciation.

Nath'l Bowditch Potter.

New York, *January*, 1911.

PREFACE TO THE FIFTH EDITION

After the fourth edition became exhausted there were so many demands for the book that the first half (on physical diagnosis) was revised and published first. The rest of the fifth edition is now completed. The many alterations and additions delayed its appearance longer than desirable, but this may be excused because of the great amount of work necessarily connected with revision. As in earlier editions I have aimed to pay equal attention to all departments of internal medicine, for any specialization, aside from those departments which must be separate on account of their special surgical technic, is, in my opinion, unwarranted and injurious to the consistent and symmetric training of the physician.

The chief changes in the first half, which appeared last year, concern the following points:

The chapter upon icterus has been rewritten, emphasizing Géraudel's investigations, which have opened up new avenues of thought in the pathology of this condition. The section upon edema has also been thoroughly revised in the light of the studies of Meltzer and Starling. An entirely new section has been introduced upon the determination of the cutaneous electric resistance, a subject which is of special diagnostic importance in exophthalmic goiter. The section upon our conception of the nature of fever and the principles involved in its estimation has been rewritten, and has been made to harmonize with my clinical teachings in reference to the general pathology of fever. These I have been unable to publish in detail, owing to lack of time. A brief section upon the teleology of the various forms of dyspnea has also been introduced. This explains the accurate adaptation of the dyspnea to the particular respiratory obstruction to be overcome. It should counteract the objections made by those who have recently taken such delight in criticizing any teleologic observation. The section upon the graphic records of types of respiration in disease is also new, and is based chiefly upon Hofbauer's investigations.

The chapter upon hemodynamics has been completely rewritten. In the study of the condition of the arterial wall mention has been made of Bäumler's works, which have done much to restrict the erroneous diagnosis of general arteriosclerosis. In the sections upon tachycardia and bradycardia the so-called pseudotachycardia and pseudobradycardia have also been described. Under palpation of the pulse the use of varying degrees of pressure (dynamic palpation) to determine the strength of the pulse has been advised,—an attempt to rehabilitate a conception which has most unjustly become obsolete in modern medicine. In the new section upon my sphygmobolometer the subject of sphygmobolometry has been placed upon an accurate physical foundation, and, to my mind, the quality of the pulse has been made to furnish additional information of theoretic and practical diagnostic importance. The chapter upon sphygmography has been enlarged by a description of a number of procedures, including the method of taking simultaneous records. The following instruments have been described—the new Jaquet cardiosphygmograph and a simplified form of the same instrument, Mackenzie's polygraph, Runne's new sphygmograph holder, and an appliance of my own to utilize Jaquet's sphygmograph as a small clinical kymographion for vertical writing. In the section upon the interpretation of sphygmograms the negative sphygmograms described by Mackenzie as a source of error have been considered, and the section on the influence of respiration upon the sphygmogram has been partly rewritten and illustrated by new curves. A new chapter describes the employment of simultaneous records of the pulses of different arteries in the diagnosis of aortic aneurysms, and of narrowing of the principal arteries at their origin from the aorta. The modern analysis of the irregular pulse, included in the appendix of the last edition, has been incorporated in the text of the present volume. The discussion of this subject has been enlarged in many respects, and particular reference has been paid to Mackenzie's recently published studies. It has also been differently subdivided and illustrated with many new figures, most of them from Mackenzie, to whom I wish

to express my sincere thanks for permission to use his tracings. It has also been necessary to change radically the section upon sphygmomanometry, because many new facts have been added to our knowledge of this subject since the appearance of the last edition. A new section discusses the frequently misunderstood significance of the arterial maximum pressure, another the absolute sphygmogram, or the separate determination of the maximum and minumum pressure, the so-called pulse pressure, and the blood-pressure quotient. Further additions comprise the brief sections upon the measurement of the venous and of the capillary pressures. The chapter upon the venous pulse has been subjected to a thorough revision. The ventricular venous pulse, resulting from auricular paralysis and without tricuspid insufficiency (Mackenzie), and the transition forms between ventricular and auricular venous pulses have been described. The latter, though little noted in the literature, occur frequently. The tendency to lay too much stress upon every little wave of the venous pulse has been criticized.

In the chapter upon percussion a special section has been devoted to Selling's and R. Geigel's recent investigations upon the theory of the percussion note. In the explanations of dulness, particularly deep dulness, I felt it incumbent upon me to go somewhat deeply into details, since it seems that considerable confusion is apt to result here from misconceptions of physical laws. The effects of this confusion are experienced in practice, since unwarranted attempts are made to discredit methods of percussion which seem to me sufficiently well founded. I must, consequently, take up my position in reference to the more recent modifications of the method of percussion. ("Schwellenwert" percussion, orthopercussion, etc.) In the description of the topographic percussion of the lungs and of the heart, Moritz's and Dietlen's orthodiagraphic investigations have been mentioned, and although praiseworthy, they have been considered purely as anatomic studies in the living. I do not agree with these authors that this method will influence or modify in any way the results of percussion which have been accepted for years. In the description of pleuritic dulness I endeavored to interpret correctly Rauchfuss's paravertebral triangle of dulness, as well as the recently resurrected Garland's or Damoiseau's outline of dulness in pleurisy. In the discussion of mediastinal dulness mention has been made of that due to fat and described by von Hampeln. To assist in the early diagnosis of tuberculosis a section has been introduced upon the demonstration by percussion of a diminished respiratory expansibility of partially infiltrated portions of the lung. The theory of cog-wheel respiration has also been revised.

In the chapter upon auscultation a section has been devoted to the graphic recording of the cardiac sounds and to the chronoscopic determination of the length of the systole. This determination is based upon the employment of a new pocket chronoscope, constructed by Hipp, in Neuchatel, according to my specifications. With this instrument, described here for the first time, hundredths of a second may be directly read.

The section upon the cardiac impulse gives a detailed description of the diagnosis of cardiothoracic adhesions. It introduces the subject of cardiolysis, and is based particularly upon Brauer's investigations. In view of the new graphic instruments described in this edition, the technic of cardiography has been more minutely set forth than heretofore.

In the chapter upon palpation the importance of the Trendelenburg position is emphasized. In reference to appendicitis an attempt has been made, upon the basis of Nothnagel's and Meltzer's investigations, to throw some light upon the nature of the colic. Unfortunately, this could not be done as fully as I could wish, in view of the practical importance of the subject. The decadence of this portion of diagnosis, as a result of superfluous surgical operations, furnishes a sad and highly culpable tendency of the twentieth century.

The section upon the compensation of cardiac diseases notes some new principles and points of view in reference to the explanation of hypertrophies and dilatations.

In the second half of the completed work the revision and amplification have been extensive. Only the most important innovations can be mentioned here.

In the section on the examination of the stomach the diagnostic value of the more recent statements, in regard to the size and position of the stomach obtained by orthodiagraphy, has been estimated. The desmoid test, suggested by the author, has been discussed more minutely. For, in spite of all the objections in the literature, this method has proved valuable in my clinic, providing in the given case the point at issue be rightly taken. The objections are based on a misunderstanding of what the method can and will do. I have recently adopted F. A. Hoffmann's method for estimating the ion-concentration of the gastric juice by the determina-

tion of the rapidity of the decomposition of methyl acetate by its free hydrochloric acid. I have added to the methods of pepsin determination mentioned in the last edition those of Volhard, Jakoby, Fuld, and Gross, as well as the refraction method worked out in my clinic by G. Schorer. Grützner's almost forgotten carmine method, simple and elegant enough to be permanent, has been more fully credited. In regard to the clinical use of the pepsin determination methods, some of the present procedures for the absolute pepsin determination have been established as anomalous points of view. Blum's, Fuld's, and Volhard's recent methods for estimating lab-ferment are fully described, as well as Salomon's test for the early diagnosis of gastric carcinoma. Sufficient suggestions for the bacteriologic testing of the gastric contents have been added, and the value of the dry and bouillon test meals, first described by me, has been discussed. It is hoped that the use of a small butyrometer adapted to the ordinary clinical centrifuge, and the resulting simplification of butyrometry of the gastric contents, will finally answer the unwarranted objections to this procedure. I have shown that the stomach can be completely emptied without lavage by a little-known method (employing a tube with several fenestra and a low position of the cardia), which I have long used and which has been published four years. This, among other things, has been responsible for discrediting Matthieu's procedure for determining the residue, to which many just objections have been raised, and which has been quite discarded in favor of the butyrometric method. I have often emphasized this in the debates over the gruel; but the writers, who believe that a method of gastric examination of more than twenty years' standing cannot be bettered, continue their futile opposition. It is hoped that the collected statements in this book will prove sufficient to convince the opponents of this method of its superiority. For them chiefly is meant the section on the criticism of the method. A new section on the demonstration of the most important poisons in the gastric contents is introduced.

The chapter on examination of the intestines has been much enlarged. Modern rectoscopy has led to such great advance in the early diagnosis of high rectal carcinoma that it should be as completely mastered by the average physician as laryngoscopy. It has been discussed at length. The wrong judgment of the value of the glutoid test, so frequently mentioned in the literature, has been properly set forth. Schmidt's nucleus test, and the extraction of intestinal juice suggested by Volhard-Boldireff, are discussed. In the sections on intestinal parasites, the new species described in the literature have been included, *e. g.*, Ascaris mystax, Schistosoma japonicum, the many recently described, rare forms of Tenia and Bothriocephalus cordatus, and the occurrence in the intestinal contents of moth and fly larvæ (Myasis intestinalis) has been mentioned. The question of the use of test-nourishment, in the examination of the feces for determining the intestinal functions, has been critically discussed in a manner differing from the present practice. The technic of Schmidt's and Strassburger's fermentation test has been described. The section on the bacteriology of the intestinal contents is enlarged, and more recent methods for detecting blood in the feces are presented.

Numerous additions and improvements have been made to the section on urine examination; thus, in the appendix the Lambotte separator and my new simplified model have been described. The use of these improved instruments renders ureteral catheterization superfluous in the majority of cases. Physiologic and functional albuminuria have been discussed at length. The methods for differentiating serum albumin and globulin and the determination of F. A. Hoffmann's albumin quotient, as well as new methods for quantitative determination of albumin, such as the refractometer method of Schorer, Dénigé's titration and diaphanometric method, and the estimation of the albumin content by means of Tanret's reagent have been described. The so-called Bence-Jones albumosuria and the detection of the Bence-Jones proteid, as well as the vexed question of those urinary proteids which are precipitated by acetic acid in the cold (mucin, nucleo-albumin, euglobulin, Mörner's albumin compound and nucleo-histon), are exactly described. New tests for blood in the urine, Ehrlich's paradimethylamidobenzaldehyde reaction for urobilinogen, Malfatt's milk-sugar reaction, Cammidge's reaction, and Lange's acetone reaction have been included. Tests for new substances have been included in the section on the detection of drugs and poisons in the urine. New methods for the quantitative estimation of sugar have been described, especially my useful modification of Pavy's method, the Gerard-Williamson titration method, and Wagner's exact fermentation saccharometer. All the more recent methods for determining urea, uric acid, and purin bodies known to me have been included, as well as Strauss's method for the quantitative estimation of indican, and the Folin-Gottlieb quantitative kreatinin determination. At the request of my French

colleagues, Bourget's phosphatometer has been described, and, in this connection, the nature of phosphaturia has been discussed as in the last edition. Sections on the quantitative estimation of ammonia, acetone, and oxybutyric acid have been made more complete by the addition of new methods.

The section on the bacteriologic examination of the sputum has been revised. I may merely mention here the discussion of the non-acid fast form of tubercle bacillus, the so-called tubercle bacillus fragments, the researches of Ellerman and Erlandsen on the improvement of methods of sedimenting for the demonstration of tubercle bacilli, the description and discussion of Bordet's whooping-cough bacillus, and the differentiation between streptococci and pneumococci and the virulent and non-virulent forms of streptococci.

The revision of the chapter upon the blood has perhaps been the most thorough of all. A complete exposition is made of the new methods for estimating the mass of the blood. In the discussion of the reaction of the blood, mention is made of Hamburger's alkali titration method, especially of the titration of the diffusible alkalies, as well as Friedental-Schultz's estimation of ion-concentration. New methods are presented in the sections on the coagulability of the blood and on hemaglobin estimation. Here, also, are suggestions concerning my hemometer, especially as to its standardization, in regard to which mistaken views are widespread, in spite of the complete directions for use given with the instrument. In this section conception of masked chlorosis has been introduced. The chapter on counting the blood-platelets has been altered. Hagen's hematimeter and Bürker's counting chamber have been described. A section on the practically important question of counting the blood-paltelets at a distance from the bedside has been inserted. The original form of hematocrit was justly discredited. It has been rehabilitated here on account of improved and correct methods. The section on testing the resistance of the red cells to hypo-osmotic or other injury has been altered, and here the methods of Hamburger and Ribierre and their interesting results, especially in different forms of icterus, are discussed. Giemsa's, Leishman's, the panoptic-triacid, and Ehrlich-Lazarus iodin-eosin methods of blood staining have been completely described. The Cabot-Schleip ring forms are described. The behavior of the blood in infectious diseases (leukocytosis, leukopenia, eosinophilia, lymphocytosis) is much more exhaustively discussed than before, and those diseases in which the blood findings have recently become known are mentioned (small-pox, measles, typhus, relapsing fever, dengue, Malta fever, rabies, tetanus, actinomycosis, syphilis, trichinosis, etc.). Ziegler's, Schindler's, and Arneth's studies on the qualitative changes of the leukocyte blood-picture in infectious diseases are discussed, as well as Neisser's researches on lipemia. The more recent investigations on trypanosomes, spirochetæ, piroplasmata, and warm embryos are discussed and explained by illustrations. The primary blood diseases are much more fully treated than formerly, and the very voluminous literature and my own experience are both made use of. O. Näglei's excellent work on blood diseases and blood diagnosis was found especially valuable in this connection, and from it, with his permission, the plates of the myeloblasts described by him were reproduced. In the section on pernicious anemia I have advanced the theory that this disease is a consequence of diminished hydrochloric acid in the gastric juice and the resulting diminution in the absorption of iron. I have mentioned this in my clinic for years, but this is the first time I have published it. The section on lymphomatosis is altered. More recent observations on the blood in Banti's disease, multiple myeloma, purpura, scorbutus, Barlow's disease, hemophilia, myxedema, Basedow's disease, malignant tumors, paroxysmal hemoglobinuria, lead and phosphorous poisoning, icterus, asthma, and burns have been presented. The new methods for the estimation of the viscosity of the blood have been included, as well as those for the quantitative estimation of serum albumin, the detection of potassium cyanide and prussic acid, the quantitative estimation of uric acid, the oxydase reaction, and the examination of the blood for bile-pigment and urobilin. The agglutination reactions of the blood have been revised, and the examinations of the bactericidal power of the blood and the Wassermann-Neisser-Bruck serum reaction in syphilis have been included. This chapter has been enriched by two excellent color plates.

The sections on the examination of the alimentary canal have been exhaustively revised. I would mention particularly the detailed discussion of the examination of the esophagus by the Röntgen rays, and of esophagoscopy, in which Brünings' new broncho-esophagoscope is described. The special findings in each affection of the esophagus are exhaustively described, and Neisser's sound palpation of tuberculous bronchial glands also referrd to. The chapter also contains a description of two recently devised sounds—a diverticulum sound and a dilatation sound.

I have included in the chapter upon rhinoscopy a number of cuts of rhinoscopic findings in empyema of the accessory sinuses which are of great practical importance.

The section upon exploratory punctures is considerably enlarged. Here special attention is directed to the more detailed presentation of cytology of the puncture fluids, to the discussion of the existence of proteolytic ferment action of the exudates, to the elaboration of pressure determination in pleural exudates, and to a chapter on exploratory cranial puncture, introduced especially by Neisser and Pollack.

The sections on examination of the nervous system also contain many additions, all of which cannot be mentioned here. For example, testing of the sensory effect of faradic vibrations and of muscle contraction (Curschmann); discussion of Rautenberg's discovery of the alternating contractility of muscles under electric stimulation, as well as of myautonomy, also described by Brautenberg; and of some remarks on condensator discharges. The psychogalvanic reflex phenomena, described by Veraguth, is briefly alluded to.

The section on aphasia has been thoroughly revised, and the isolated alexias and agraphias more exhaustively considered than in the earlier edition. P. Marie's conception of aphasia is criticized adversely, and its consideration furnishes the opportunity of introducing a conception of logasthenia. Several new diagrams cast fresh light on aphasia. Localization has been amplified by the introduction of a series of new cuts. In all the chapters dealing with the examination of the nervous system I have endeavored to explain the pathologic symptoms by physiologic facts, *e. g.*, in showing at length the connection between the stasis of nervous excitation and physiologic chorea, physiologic trembling, etc. The more recently described "Phenomena," reflexes, etc., are given as faithfully as possible, in so far as they have come to my knowledge.

Finally, it need hardly be remarked that, besides the more important changes and additions which are mentioned above, and which are partly comprised in new chapters (compare the systematic index), numerous details, both of form and style, have been altered, and considerable new material, based on my own observations, and hitherto unpublished, has been added.

Owing to all these additions, the book is enlarged by about 300 pages, the number of cuts increased from 291 to 389, and the number of plates from 5 to 7. The work would have been still larger, and exceeded one volume, were it not condensed by omitting many of the older and more or less disputed methods. Experience teaches us, however, that there are false as well as true advances in medicine, and that, in our rapidly moving age, the established good is sometimes forsaken for short-lived theories. I would, therefore, recommend the possessors of earlier editions to keep them, since they contain many useful methods which will again come into good repute. I think it necessary to emphasize this point, although I have taken great pains in the critical selection of material, and have tried to present what I personally have found to be of the greatest value at the present time.

One word more in regard to my attitude upon the Röntgen ray diagnosis. The invaluable early enlightenment which we owe to this method is given full credit throughout the new edition. Compare, in particular, the chapter on percussion of the heart; on the position of the stomach and the examination of the alimentary canal. On the other hand, I am still opposed to including the Röntgen technic in a book of this character. I have selected chiefly methods the technic of which I have personally mastered, and such as can be expected to be within the grasp of any trained physician of the present day. The Röntgen technic itself does not come under this head. It is true, I frequently make use of Röntgen ray examination in my clinic, but the technic is managed by a specially provided Röntgen ray expert. I do not consider myself qualified, therefore, to instruct others in this technic. A mere compilation of Röntgen technic, which naturally I could review only superficially, does not enter the scope of this book, as it is intended chiefly to describe my own methods of work.

The arrangement in my clinic alluded to above is in conformity with the fact that, despite a progressively increasing demand for the rounded education of physicians, it can scarcely be expected that every practitioner should be a master of the Röntgen technic. Nor is this a disadvantage. Examination with the Röntgen ray plays in internal medicine, as in my clinic, the part of a referee in difficult questions, but is not to be resorted to at first, and not in all cases, but only when other methods of examination are unsatisfactory; and, according to my opinion, this is the position it should continue to occupy. According to this, instruction in the Röntgen technic should remain the province of special courses and special textbooks. I contend that it is no sign of progress when the Röntgen method super-

sedes to too great an extent the other methods of examination in a medical clinic and exceeds its function as a court of final appeal.

In the first place, the Röntgen ray examination is not adapted to many, and especially the commonest problems which the older methods readily solve, and, hence, often leads to errors. In the second place, the necessity of a cumbersome apparatus militates against its ever becoming a principal factor in medical examination. Such a special method of examination should not, for didactic reasons, be placed in the foreground of the clinic, lest the students get quite a false impression of medicine, and become accustomed to consider Röntgen ray examination as a refuge for the lazy, which would make the tedious training in physical diagnosis superfluous. I have frequently been confronted with the lamentable diagnostic inefficiency of those physicians in whose studies the Röntgen ray examination was placed on a high pedestal, and who consequently had not thoroughly mastered the art of percussion. These unfortunate persons remind me of certain candidates who, in an examination on tuberculous meningitis, knew nothing except that it could be diagnosed by lumbar puncture and the demonstration of tubercle bacilli in the cerebrospinal fluid. What could such a physician do in practice! If, in clinical instruction, we exaggerate the importance of Röntgen ray examination, we offer the student a stone for bread. For what can a practitioner do with it if he have a small practice in the country or in a mountain village? And yet we must train physicians for this type of practice and turn out skilful educated practitioners. So, in this case, sense may become nonsense, and a benefit, a nuisance.

I cannot close without reiterating that this book is not a mere compilation, and that the major portion of its contents is derived from my own experience, and represents personal views and observations hitherto unpublished, which have not been sent as original contributions to the journals because my time has been insufficient, and because I am not in favor of too much medical scribbling and of manufactured articles. I mention this because the present work scarcely deserves to be quoted from. This is explained by the fact—and it is to the detriment of an harmonious progress in medicine—that medical literature of the present day is almost exclusively sent to journals. Besides, it is usually taken for granted that text-books, not to include the systems of medicine which are so popular to-day, and which display so many names on the title page, are merely compilations and contain nothing new. If an author has anything important and new it is assumed that he would have first marketed it among journals. My own views are quite at variance with this opinion. The following instance, among others, justifies my remarks. In the *Deutsche medizinische Wochenschrift* for 1904, p. 716, a prominent author, discussing certain mistakes in auscultating the lungs, asserted that this book was the only one of the current text-books to include a brief chapter upon the subject, "evidently based on a paper read by Treupel at the Society of Freiburg physicians." If he had taken the trouble to inform himself, he would have discovered that this chapter was almost exactly the same, even in its first edition, 1894, *i. e.*, four years before the appearance of the paper from which the data were supposed to have been gathered.

HERMANN SAHLI.

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INTRODUCTION

HISTORY AND OBJECTIVE EXAMINATION

THE first essential for correct diagnosis in any given illness is a careful account of the subjective and objective symptoms and of their manner of development. These statements, made by the patient or his relatives, are called the *history*. It may be divided into two parts: first, the history in the narrow sense of the term, including the patient's story of his illness up to the time the physician sees him; and, second, his account of his present symptoms, an account which must always be supplemented by an objective examination. The answers to the questions obtained in the history frequently furnish sufficient evidence to make a comparatively accurate diagnosis without examining the patient. Countless examples might be mentioned in illustration; for instance: A patient says that a few days before, when in apparently good health, he was suddenly seized with a severe chill and a stabbing pain in his side, and that ever since then he has been feverish and short of breath, coughing and expectorating rusty sputum. With such a story a physician would naturally make the diagnosis of croupous pneumonia.

Before attempting any objective examination, and merely by skilfully directing his questions, an experienced physician can obtain a fair idea of the disease, even in cases where the evidence is less conclusive than in the above example, although an exact diagnosis can usually be made only after completing the objective examination; for many diseases furnish only subjective symptoms. There are even cases in which the history affords the only clue to diagnosis. A ripe experience is requisite in order properly to utilize the history in making a diagnosis. A complete knowledge of the pictures of all the diseases which might enter into consideration in any given case is very essential in selecting the proper questions, as well as a keen critical power in interpreting the value of the evidence given in the history, since otherwise unessential facts might be made conclusive points in a diagnosis. Only years of experience can overcome one very constant difficulty—the varying individuality of patients. An hysterical society woman describes to her physician symptoms which, in a sturdy laborer, would be properly attributed to pathologic changes; but the adept practitioner understands that such complaints are nothing more than the expression of the peculiar, sensitive, and exaggerating mental condition of an hysteric person, and so does not lay too much stress upon their significance. Vice versâ, a stolid, callous peasant often complains very little even when afflicted with a serious disease; or, again, a patient normally sensitive may be so benumbed by a disease that he does not complain at all. In the latter instance the great contrast between the subjective well-being (euphoria) and the objective visible disease frequently suggests a very unfavorable prognosis.

Without depreciating the value of the statements of the patients and their friends, it is evident from what we have said that the methods of objective examination, with which this book is concerned, contain the most essential elements in diagnosis. Although we have illustrated the possibility and the occasional necessity of making a diagnosis merely from the history, yet we could as easily mention innumerable instances where the most skilled practitioner could not form an approximate conception of the disease without the most searching physical examination. Even in the simplest of cases no physician should neglect the precaution of examining his patient carefully, including in such an examination all the organs. For, on the one hand, some organic diseases do not excite subjective symptoms; and, on the other hand, there may be some organic changes which annoy the patient sufficiently to lead him to consult his physician, while others of the greatest importance may exist of which he has no suspicion, and which the objective examination first discloses.

Objective examination includes a number of different methods, some depending on mere observation, but others requiring especial technical, chemical, or physical aids. The beginner must very early acquire facility in all these methods of examination. Their mastery will furnish the groundwork for acquiring extended experience in clinical observation upon the symptomatology, the course, and the prognosis of disease, and for obtaining reliable data for therapy.

A FEW SUGGESTIONS FOR TAKING HISTORIES

It is very difficult to give any detailed directions which will be generally effective in taking a history. In serious diseases only an able and experienced physician is capable of performing this task thoroughly, and he will need to utilize his entire medical training. Since we shall mention in the appendix upon special diagnosis most of the methods made use of in history-taking, in the following paragraphs we need only give a few rules to serve as a framework for the beginner to broaden and build upon as his knowledge and experience grow.

Few persons are so mentally constituted as to communicate to the physician simply and directly the medically important facts of their ailments. Most patients relate a mass of unimportant matter and say nothing about the essentials, and only skilfully planned questions will prevent the patient or his relatives from irrelevancy. But a patient should never feel that he is being guided, nor that his physician does not enter with interest and sympathy into all the minute details of his trouble. Putting a mild curb upon the patient's volubility does not mean that one should concern one's self exclusively with the typical and characteristic symptoms of disease; because many things apparently immaterial in the eyes of the beginner, who knows a disease only as a scheme, have really considerable interest and a great importance. Even many conditions which have apparently nothing at all to do with the medical aspect of the case—for example, occupation, family affairs, etc.—are very helpful in comprehending the clinical picture, especially the etiology and, with it, the treatment. In short, the patient should be led to relate neither too much nor too little.

It is quite as important that the physician himself should be accurate in framing his questions. It is easy enough to ask too little, but difficult to ask too much or to question too minutely, not only on account of the multiplicity of the appearances of disease to be mastered, but even more on account of the danger of considering any important point as proved after a few hasty questions. In the author's opinion this is the most frequent and serious fault which the beginner perpetrates; *e. g.*, a feverish patient is asked if he has had a chill, because such a symptom would suggest a definite disease, pneumonia. Without much thought most patients answer this question in the affirmative; but more careful questioning develops the fact that the supposed chill is in reality only the slight chilly feelings accompanying nearly all feverish diseases. In the typical chill of pneumonia the patient's teeth chatter, and he shakes as if immersed in ice-water. This is quite a different symptom

in its diagnostic significance from the slight shivering of fever. The patient's statement that he has had a chill is not sufficient; we must inquire more particularly as to the nature of the chill. Often enough patients betray their mistake by using the word chill in the plural. Similar errors may arise from the statements patients make in regard to many other symptoms and long-standing diseases. The names they give to their former illnesses are especially apt to be incorrect and often occasion serious errors, for many are diagnoses made by the laity and many others are incorrect; *e. g.*, most cases of so-called "meningitis" which have been cured. Again, patients with tuberculosis often misname an acute exacerbation of their disease as "influenza"; further, so-called "catarrh of the stomach" is usually a manifestation of the general effect of tuberculosis. "Rheumatism" is another diagnosis which must always be looked upon a little skeptically. Frequently enough the clinical picture shows that the so-called "rheumatism" is a manifestation of tuberculosis or of pleurisy, etc. Similarly, many other names of diseases, such as "nervous fever," "joint rheumatism," "dysentery," if accepted without criticism and without minute interrogation, may lead to errors in diagnosis. The best way to avoid such mistakes is to disregard names given by the patient and to make one's own diagnosis by establishing as objectively and accurately as possible the symptoms of the preceding disease.

A further and equally serious fault is the tendency of many beginners to start from a preconceived notion of the diagnosis and to extract from the patient all possible facts in the history which will coincide with this supposed disease. To recognize this fault should be sufficient to avoid it effectually.

We can hardly ask too detailed questions as to the *influences of heredity*, inquiring accurately concerning parents, brothers, sisters, children, uncles, and aunts. An inquiry as to whether this or that disease has occurred in the patient's family will usually elicit a negative reply. To determine the facts accurately the disease in question must be quite specifically designated, possibly even a summary of the symptoms detailed. A patient may deny the occurrence of pulmonary disease in his family; but should we ask if either parent had a chronic cough, had expectorated blood, or lost a good deal of weight, we can frequently enough become convinced that one or the other suffered from tuberculosis.

In regard to neuropathic taint, we must question very accurately and particularly. For example, an epileptic will practically always deny the occurrence of any nervous disease in his family. We may, however, obtain a positive reply by asking whether his father, mother, brother, sister, uncle, or aunt was epileptic, if they had suffered from nervous attacks, or if they had been nervous or mentally affected in some other way.

If the histories be difficult to obtain or if patients contradict themselves, it is advisable to repeat questions later on, thus frequently clearing up some complicated point. The repetition of our task with stupid and prattling patients, unfortunately, obtains for us little more than renewed contradictions. Even this is a relative gain, for at least we discover how little we can trust them, and draw no false conclusions.

In general, good history-taking requires much diplomacy, tact, and knowledge of people and of medicine. A physician should never allow a patient to feel that he is in a hurry. The public considers that the physician has time for everything and everybody. Sit quietly, even if you are sitting upon hot coals, and wait for a favorable moment to interrupt, in a diplomatic way, the flow of talk. An excellent medical precept is not to fatigue a patient seriously ill with too thorough questioning, but to obtain as much as possible from the relatives, or to leave parts of the history until a later period. Furthermore, it is always advisable to discuss with the patient alone facts which he might wish to conceal from others. Finally, the beginner puts only a small part of the necessary questions, not realizing how much must be asked in order to make a complete history. Few rules can be given, but the following table will probably be of considerable service:

Scheme for History-taking

Date; personal statements (name, age, position, occupation, residence); condition, *i. e.*, married or not; complaint; onset of the present illness; a description of the symptoms in the order of their appearance.

Etiology.—More exact information about the occupation and mode of life, injuries, strains, taking cold, errors in diet, etc. Infectious diseases in the neighborhood. Previous treatment and course of disease.

Past History.—Any antecedent disease like the present. If so, course of same. Injuries. Other preceding illnesses; infectious diseases; and of these especially:

joint rheumatism, scarlet fever, measles, whooping-cough, typhoid fever, erysipelas, malaria, sore throat, gonorrhea, syphilis. Previous symptoms of disease: Edema; dyspnea; cough; expectoration; expectoration of blood; palpitation of heart; difficulties of urination and alterations in the urine; constipation; diarrhea; icterus; vomiting; vomiting of blood; abnormalities of hunger and thirst; headache; marked changes of weight. In the female sex: chlorosis; pregnancies; births; menstruation; gynecologic difficulties. All these symptoms and conclusions which the past history furnishes must be analyzed in the same way as the symptoms of the present disease. (See below, 2. Complaint.)

Heredity.

THE GENERAL ROUTINE OF AN OBJECTIVE EXAMINATION

The following plan the author considers an excellent method for a routine examination, the order of the questions being the natural and practical one. The individual observer may expand the scheme in accordance with the contents of the work in question.

1. *Expression of countenance and general deportment of the patient; voice; speech; psychic behavior.*

2. *Complaint.* (See Scheme for History-taking.[1]) *Kind of sick feeling. Weakness. Loss of flesh. Disturbances associated with the nervous system. Disturbances in connection with the organs of respiration.*

Dyspnea, constant or paroxysmal. The exciting cause of the paroxysms. Breathing slow or rapid during attack of dyspnea. Stridor, inspiratory or expiratory.

Cough, with or without expectoration. Characteristics of the expectoration. Admixture of blood. Peculiarities of the latter. Subjective sensation respecting the source of the expectoration (throat, larynx, nose).

Pain with breathing. Its location.

Disturbances in Connection with the Circulation.—Palpitation, constant or paroxysmal. Apparent exciting cause of the paroxysm (agitation, exertion, or posture). Palpitation accompanied by sensation of pain (left arm, back, epigastrium, precordia). Palpitation accompanied by dyspnea. Subjective sensation of arrhythmia (*i. e.*, tripping or skipping of the heart-beat). Edema. Amount of urine.

Disturbances of the Digestion.—Appetite. Pain. Influence of the ingestion of food and drink upon the pain (favorable or unfavorable). Time of onset of pain (soon after eating, during the night, in a fasting condition). More exact location and radiation of pain (back, right shoulder). Nausea. Vomiting. Amount and character of the vomitus (mucus, blood, food). Its taste (sour, bitter). Time of vomiting, pointing to retention or not. Belching (sour, bitter, rancid). Evidence of hemorrhoids. Constipation: Frequency of bowel movements. Character of feces: color. Large scybala, abnormally small lumps. Distention of abdomen and other discomforts when constipated. Flatulence. Diarrhea: frequency, consistence, color, amount of each dejection. Pain in defecation. Tenesmus. Bloody or slimy evacuations.

Disturbances of the Urinary Apparatus.—Urgency. Bladder or kidney pain. Radiation of the pain. Tenesmus of bladder. Amount of urine. Pollakiuria. Conspicuous qualitative changes of the urine (cloudy, bloody, smoky). Passing of stone, gravel, or sand. Phenomena of retention or incontinence. (See Examination of Bladder.)

Other Disturbances.—Fever. Night-sweats. Headache. Thirst. Insomnia, and its apparent cause.

3. *History proper*, in conformity with the above plan.

4. *Examination proper*, which should cover the following points:

Build, development, and *nutrition.*

Temperature, frequency of pulse and *of respiration.*

Characteristics of Skin.—Turgidity, color (pallor, cyanosis, icterus); eruptions; pigmentation; scaling; striæ; final confirmation of other external diseases (joint affections, erysipelas, etc.).

Head and Neck.—Mucous membranes, especially conjunctivæ, tongue, gums, pharynx, tonsils, herpes labialis, glands, goiter. Cervical veins (their dilatation or pulsation).

Respiratory Apparatus.—Dyspnea: its character; polygopnea, oligopnea, in-

[1] Similar rules apply as in taking the actual history (see above). Moreover, it is of great importance to ask directly about the symptoms enumerated here because patients themselves are so apt to think them of the least importance.

spiratory or expiratory dyspnea, stridor, shape of thorax, type of breathing, breathing excursions, diaphragm phenomenon, retraction of thorax, topographic and comparative percussion and auscultation of the lungs, fremitus.

Circulatory Apparatus.—Inspection and palpation of the precordia. Visible and palpable pulsation over that area. Location of apex-beat. Thrills. Percussion and auscultation of the heart. Exact examination of the arterial pulse. Rapidity, rhythm, fulness, strength, tension, resistance of artery wall, conformity of the frequency of the radial pulse with that of the cardiac pulsation, comparison of the pulses of different arteries. Exact examination of the venous pulse. Auscultation of the arteries. Liver pulse. Capillary pulse.

Digestive Apparatus.—Inspection and palpation of the abdomen; its shape and fulness; visible and audible peristalsis; sensitiveness to pressure, palpable tumors, resistance, peritoneal friction. Palpation and percussion of the stomach, intestines, liver, gall-bladder, spleen, and peritoneum. Inspection of the vomitus and of the feces.

Urinary Apparatus.—Manner of urination; palpation of the kidneys and bladder; percussion of bladder. Catheterization. Character of urine; amount; color; cloudiness; specific gravity; testing for albumin, sugar, and other abnormal constituents.

Special Examinations which may be Necessary or Even the Most Important of all in a Given Case.—Examination of the nervous system in accordance with the plan to be mentioned later. Rhino-, laryngo-, ophthalmo-, otoscopic examination. Testing the blood, including counting the corpuscles, estimating the hemoglobin, and the microscopic examination of the fresh and stained blood. Microscopic examination of the sputum, of the urine, of the vomitus, and of the feces. Bacteriologic examinations. Sphygmography, sphygmomanometry, and sphygmobolometry. Examination of the esophagus. Examination of the stomach by means of the stomach-tube (distending with gas, a test-meal, the determination of the motor power of the stomach by distention with water). The desmoid and glutoid reactions. The examination for pyloric stenosis by means of cork capsules. Distention of the colon to determine the location of tumors. Examination of the rectum. Of the male and female genitalia. Exploratory punctures.

It is the province of special pathology or of special diagnosis to interpret the signs of disease discovered in this manner, to correlate, and to unify them into a definitely conceived disease of etiologic, functional, or anatomic nature.

GENERAL CONDITION OF THE PATIENT

POSTURE IN BED

The general deportment of the patient is the first thing which attracts our attention and influences our judgment as to his condition. In many cases even the patient's relatives will reveal whether the illness is serious or slight. Ordinarily, physicians see seriously sick patients in bed, while those with slight ailments walk about. Yet there are countless exceptions. Sometimes seriously ill patients go to bed only as the last extremity; and, as is well known, patients may walk about even during the height of typhoid fever or pneumonia. Vice versâ, many patients take to their beds on account of very slight ills. These peculiarities depend upon the social position and the employment of a patient, and upon the great difference in the individual susceptibility to sickness. Besides, we must remember that even very slight ailments which always run a favorable course are sometimes associated with such distressing symptoms that the patient is compelled to take to his bed. Despite such exceptions, we may say that certain diseases necessitate rest in bed, others are ambulatory. Patients with the acute exanthemata are commonly found in bed by the physician because they feel very ill. The same is true of circulatory disturbances, peritonitis,

meningitis, pneumonia, and acute inflammatory rheumatism. It is ordinarily easy enough to determine whether the patient keeps his bed on account of feeling ill, weak, and perhaps feverish, on or account of dyspnea, pain, or other difficulties, which are increased by walking about.

THE EXPRESSION

The expression is of great diagnostic importance, enabling the skilled physician to draw conclusions as to the subjective feelings and the mental condition of the patient. The terms commonly applied to the expression—suffering, anxious, painful, careworn, uneasy, very ill, agitated, dulled, stupid, flustered—are perfectly plain without further explanation. Feverish patients present a characteristic appearance; sometimes they have a peculiar animated look, at other times an exceptional depression of the mimic faculty, often combined with glistening eyes, a feverish redness, and an increased turgidity of the skin of the face. The facial expression of a patient suffering from dyspnea is quite as distinctive, it being dependent upon peculiarities in the appearance of the skin (cyanosis, edema) and upon the mimic elements. The dilatation of the nares (see later), combined with the open mouth, is especially characteristic. (See p. 50 for a description of the typical *facies Hippocratica.*) The unusual expression of tetanus, called the *risus sardonicus* (sardonic laugh),[1] has been variously described. While the mouth is distorted as in laughing, the upper part of the face, especially the brow, is wrinkled, just as in the expression of trouble or sorrow. Tetanus poison apparently contracts the muscles of the entire facial territory and causes a combined stimulation of practically antagonistic muscles.

MENTAL CONDITION

A patient's facial expression and his demeanor during our questioning furnish the best means of estimating his mental condition.

ACTIVE AND PASSIVE POSTURE IN BED

A critical observer obtains diagnostic points by noticing the position which the patient assumes in bed. The less the general feelings are affected, the more natural and unconstrained is his pose. He tosses about, pushes the pillows straight, and shifts his attitude when one position has become uncomfortable. This is called an active position in bed (active dorsal or lateral posture). On the contrary, very weak, helpless, or unconscious patients appear very different. Their attitude is lax, essentially controlled by the laws of gravity. Should such a patient slide down against the footboard, he would remain lying there, for he is incapable of drawing himself up, even if the position be very uncomfortable and his breathing embarrassed. This is called a passive position in bed (passive dorsal or lateral posture).

CONSTRAINED ATTITUDES

Some very characteristic postures are almost diagnostic of certain diseases. For example: respiratory, cardiac, or renal affections associated with much dyspnea prevent a patient from lying upon his back: in

[1] This name is derived from "sardone," a poisonous plant of the ancients, the ingestion of which produced such an expression.

the first place, because the accessory muscles of respiration can be used to advantage only in the sitting posture, with the spine fixed and sometimes the arms; in the second place, because, if fluid has accumulated in the abdominal cavity, the sitting posture partially relieves the diaphragm of its pressure;[1] and finally, because the influence of gravity possibly relieves the venous congestion of the brain and of the respiratory center in particular. With extreme dyspnea, the so-called "*orthopnea*," a patient cannot lie down, but, exhausted, is obliged to sit erect, bracing himself with his elbows and forearms upon the arms of his chair in an endeavor to utilize the accessory muscles of respiration and, if fluid be present in the abdomen, to avoid pressure of the anterior surface of the thighs upon the distended abdomen. It is worth remembering that the accumulation of a considerable quantity of blood in the veins of the lower extremities may afford some relief to the lungs and the heart, so that elastic bandages around the legs, temporarily shutting off a con-

Fig. 1.—Case of cerebro-spinal meningitis. Photograph taken from above; patient lying asleep. Marked retraction of neck, flexion of thighs and legs (Harlem Hospital, Dr. R. G. Wiener).

siderable amount of venous blood, may enable the patient to lie down, even though for a very short time.

Constrained lateral positions are very suggestive, for they almost always depend upon unilateral affections of the thoracic viscera. If, on account of pulmonary consolidation or of compression by a pleural effusion, the function of one lung be abolished, the patient usually lies upon the affected side, in order to afford the sound lung the freest possible expansion. Should there be much pain, such a position is generally reversed, because the weight of the body increases the pain; but sometimes when the pain depends practically upon the breathing the patient will lie upon the affected side, and so limit the respiratory excursion by partially fixing the painful side with the body weight. In heart disease,

[1] Except, of course, when an enormously distended abdomen is crowded by the thighs in the sitting posture.

and sometimes in health, one side is more comfortable than the other to lie on. The position which dislocates the heart, the great vessels, and the mediastinum most, thereby rendering the breathing difficult, will be avoided. Lying on one side will sometimes relieve a patient who is perpetually tormented with a cough when in the dorsal decubitus. As one can easily imagine, with constantly renewed secretion in pulmonary cavities certain positions will aggravate a cough if the secretions are being continually poured out upon the healthy bronchial mucous membranes. In some positions the cavity would become entirely

Fig. 2.—Adiposity: The enormous accumulation of fat over and within the abdomen simulates a collection of ascitic fluid.

filled before any overflow would excite the paroxysm of coughing. The latter then completely empties the cavity, thus affording the patient a temporary rest. The diagnosis of a cavity would be strongly suggested by such a history.

With colic, with cardialgia, and sometimes with intestinal obstruction patients generally prefer to lie upon the abdomen, because the tension of the distended intestines is diminished or their position shifted and the pain relieved; but in peritonitis the abdomen is so sensitive to pressure that the dorsal decubitus is assumed. On account of the epigastric tenderness, it is comparatively rare to find a patient with a gas-

tric ulcer lying upon the abdomen, unless such a position frees the ulcer from the contact or pressure of the gastric contents, *e. g.*, if situated upon the posterior wall. Patients with headache sometimes prefer to lie upon the abdomen. The characteristic positions of patients suffering from cerebrospinal meningitis or wry-neck depend upon cramp-like contractions of certain groups of muscles; some peculiar paralytic positions, upon paralyses of muscles.

GAIT AND ATTITUDE

An alert, erect attitude and a rapid walk usually signify good physical condition, while a stooping, relaxed posture with a slow, fatigued gait indicates that the person is seriously ill or mentally depressed. (For a description of various gaits characteristic of definite nervous diseases see Examination of the Nervous System.)

DEVELOPMENT AND STATE OF NUTRITION

A robust, vigorous, or muscular physique means that the bodily dimensions are rather above the normal, whereas a weakly or puny physique would indicate the contrary. The subcutaneous fatty layer (panniculus adiposus) is perhaps of even more importance than the muscles in estimating the state of nourishment. The former varies within normal limits in accordance with the age, sex, and occupation of patients. Corpulence is generally associated with a weak musculature. Nursing infants possess an extremely well-developed layer of fat; during childhood it gradually diminishes, and in the third or fourth decade increases again, while at old age it finally diminishes. A marked tendency to corpulence is often observed in women, especially after the menopause.

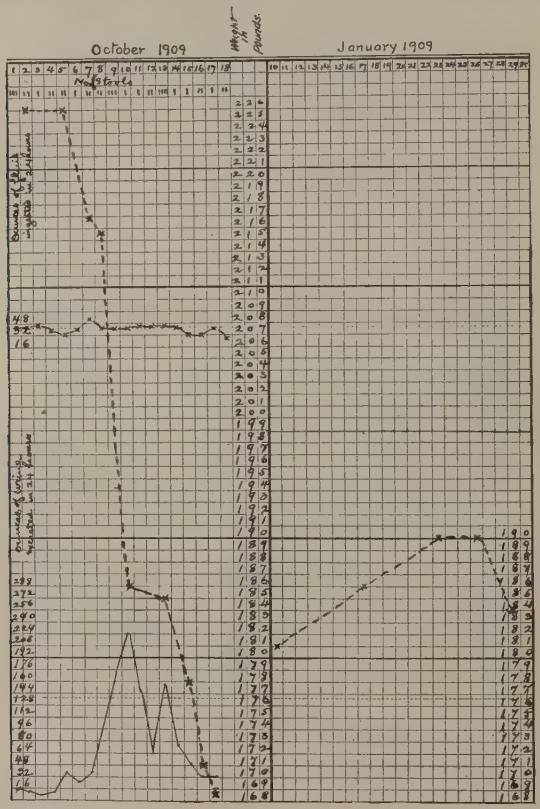
Fig. 3.—Pronounced emaciation in a chronic disease. Case of multiple myeloma (New York City Hospital).

Most chronic diseases are accompanied by a noticeable deterioration of the general nutrition. This is due either to lack of appetite, and, hence, insufficient food, or to defective assimilation, or to excessive combustion of the food assimilated. Emaciation is particularly evident in chronic febrile and digestive diseases, and becomes most pronounced in severe and prolonged typhoid fever, in phthisis, in carcinoma, especially esophageal carcinoma, and in certain cases of diabetes mellitus. In these diseases the musculature suffers a loss almost as rapidly as the fatty tissue. Marked emaciation nearly always suggests chronicity.

From a diagnostic standpoint van Noorden believes that lack of exercise incident to such patients' symptoms is more responsible for fat accumulation than any inherent deficiency of their oxidizing powers. Typical examples are the pronounced panniculus adiposus usually observed in chlorosis and in pernicious anemia. These diseases are not accompanied by emaciation unless the digestion is decidedly affected and food ingestion consequently limited or some other complications are present. The appearance of an anemic patient emaciated from gastric carcinoma is, therefore, strikingly different from that of a case of pernicious anemia—a point of the greatest importance in the frequently difficult differential diagnosis of these two conditions.

BODY WEIGHT

Observation of weight over a certain length of time furnishes an excellent guide to the state of nutrition. Minute cautions in regard to



[Fig. 4, A.—Free diuresis in a nephritic with marked anasarca and fluid in both pleural cavities, selected from the editor's service at the New York City Hospital. The patient excreted about 72 pints of urine and lost 58 pounds.

Fig. 4, B.—An ominous increase in the weight of a patient with mitral and tricuspid lesions and a pulsating liver, selected from the editor's service at the New York City Hospital. This patient was walking about the ward when compensation failed; he was ordered to bed on January 25, and with rest, purgation, and cardiac tonics he began to lose weight and compensation was promptly established. Each square represents 16 ounces of fluid or 1 pound of weight.—Ed.]

the accuracy of the scales, weight of different clothes, etc., are hardly necessary to enumerate. Unless accurately estimated, the weight is of no value. It is more accurate to weigh the body always either before or after eating, since a hearty meal will often make a difference of one or more pounds. General edema or the accumulation of fluid in one of the large serous sacs will considerably increase a patient's weight, while free catharsis, diuresis, or diaphoresis will rapidly diminish it. Daily weighing in these cases furnishes very good evidence of the progress of the disease.

Infants should be weighed daily or weekly, to keep track of their nutrition. The normal weight of the newborn is (females) 3000 gm. (6 lbs.) to (males) 3500 gm. (7 lbs.) (Uffelmann). During the first three or four days of life there is a physiologic loss of 200 to 300 gm. ($\frac{1}{2}$ lb.). Gerhardt[1] cites the following table:

Daily increase in	1st	month	25	gm.	Daily increase in	7th	month	15	gm.
" "	2d	"	23	"	" "	8th	"	13	"
" "	3d	"	22	"	" "	9th	"	12	"
" "	4th	"	20	"	" "	10th	"	10	"
" "	5th	"	18	"	" "	11th	"	8	"
" "	6th	"	17	"	" "	12th	"	6	"

Quetelet's[2] table [from which the following has been constructed.—Ed.] does not take into account the weight of the clothes, which has been estimated to be in men about $\frac{1}{18}$ and in women about $\frac{1}{24}$ of the total weight, although, of course, such figures must vary considerably.

Year.	Male.					Female.				
	Weight.		Height.			Weight.		Height.		
	Kg.	Lbs.	Cm.	Ft.	In.	Kg.	Lbs.	Cm.	Ft.	In.
Newborn	3.1	6.83	50.0	1	10	3.0	6.61	49.4	1	8
1st	9.0	19.84	69.8	2	4	8.6	18.96	69.0	2	4
2d	11.0	24.25	79.1	2	8	11.0	24.25	78.1	2	8
3d	12.5	27.56	86.4	2	10	12.4	27.24	85.4	2	10
4th	14.0	30.86	92.7	3	0	13.9	30.64	91.5	3	0
5th	15.4	33.93	98.7	3	4	15.3	33.73	97.4	3	2
6th	17.8	39.24	104.6	3	6	16.7	36.82	103.1	3	6
7th	19.7	43.43	110.4	3	8	17.8	39.24	108.7	3	8
8th	21.6	49.62	116.2	3	10	19.0	41.89	114.2	3	9
9th	23.5	51.81	121.8	4	0	21.0	46.30	119.6	3	11
10th	25.2	55.56	127.3	4	2	23.1	50.93	124.9	4	1
11th	27.0	59.52	132.5	4	5	25.5	56.22	130.1	4	4
13th	33.1	72.79	142.3	4	10	32.5	71.65	140.0	4	8
15th	41.2	90.83	151.3	5	0	40.0	88.18	148.8	4	11
17th	49.7	109.37	159.4	5	4	46.8	103.18	154.6	5	1
19th	57.6	126.98	165.5	5	6	52.1	114.86	157.0	5	2
20th	59.5	131.17	167.0	5	7	53.2	117.28	157.8	5	2
25th	66.2	145.94	168.2	5	7	54.8	120.81	157.4	5	2
30th	66.1	145.72	168.6	5	7	55.3	121.91	158.0	5	2
40th	.....	.....	168.6	5	7	.....	.....	158.0	5	2
60th	61.9	136.46	167.6	5	7	54.3	119.71	157.1	5	2
70th	59.5	141.17	166.0	5	6	51.5	113.54	155.6	5	1

[1] Gerhardt, Lehrbuch der Kinderkrankheiten, 1881, p. 2.
[2] Anthropométrie, 1870.

As a mnemonic aid, Quetelet gives us the rule that the healthy male adult should weigh as many kilos as his height in centimeters exceeds one meter. The female's normal weight is somewhat greater. During childhood this rule does not apply.

In the author's opinion such rules are quite arbitrary since the relationship varies both with the race and with the individual. This he emphasizes because he is convinced that such rules easily become dogmas and thus cause the layman as well as the physician to indulge in a rigid dietetic régime to bring the body-weight into accord with the accepted standard. Such a course only too frequently results in injury to a previously healthy individual.

MENSURATION

An individual's general development must be judged by a comparison between his age, weight, and height. [The following tables, based on the so-called "Nylic Graphic Table," are useful. They are correct to one pound.—Ed.]

WEIGHT TABLE (MALE)

Age.	57 Ins.	58 Ins.	59 Ins.	60 Ins.	61 Ins.	62 Ins.	63 Ins.	64 Ins.	65 Ins.	66 Ins.	67 Ins.	68 Ins.	69 Ins.	70 Ins.	71 Ins.	72 Ins.	73 Ins.
20	104	108	111	114	117	121	125	128	132	136	140	144	149	153	158	163	167
21	105	108	111	115	118	122	125	129	133	137	141	145	150	154	159	164	168
22	106	109	112	116	119	123	126	130	134	138	142	146	151	155	160	165	169
23	106	109	113	116	119	123	127	130	135	138	143	147	152	156	161	166	170
24	107	110	114	117	120	124	128	131	136	139	144	148	153	157	162	167	171
25	108	111	114	118	121	125	128	132	136	140	144	149	154	158	163	168	172
26	108	111	115	118	122	126	129	133	137	141	145	150	154	159	164	169	173
27	109	112	116	119	122	127	130	134	138	142	146	150	155	160	165	170	174
28	109	112	116	120	123	127	130	134	138	142	147	151	156	161	166	170	175
29	110	113	117	120	124	127	131	135	139	143	148	152	157	162	167	171	176
30	110	114	117	121	124	128	132	136	140	144	148	152	157	162	167	172	177
31	111	114	118	121	125	129	132	136	140	145	149	153	158	163	168	173	178
32	111	115	118	122	125	129	133	137	141	145	150	154	159	164	169	173	179
33	112	115	119	122	126	130	133	138	142	146	150	155	159	164	170	174	179
34	112	116	119	123	126	130	134	138	142	147	151	155	160	165	170	175	180
35	112	116	120	123	127	131	134	139	143	147	152	156	161	166	171	175	181
36	113	117	120	124	127	131	135	139	143	148	152	156	161	166	172	176	181
37	113	117	120	124	128	131	135	140	144	148	153	157	162	167	172	177	182
38	113	117	121	124	128	132	136	140	144	149	153	158	162	167	173	177	183
39	114	118	121	125	129	132	136	141	145	149	154	158	163	168	173	178	183
40	114	118	122	125	129	133	136	141	145	149	154	158	163	168	173	178	184
41	114	118	122	125	129	133	137	141	146	150	154	159	164	168	174	179	184
42	115	118	122	126	130	133	137	142	146	150	155	159	164	169	174	179	185
43	115	119	123	126	130	134	138	142	146	151	155	160	165	170	175	180	185
44	115	119	123	126	130	134	138	143	147	151	155	161	165	170	175	180	186
45	116	119	123	126	131	134	138	143	147	151	156	161	165	170	176	181	186
46	116	119	123	127	131	135	139	143	147	152	156	161	166	170	176	181	186
47	116	120	124	127	131	135	139	144	148	152	157	161	166	171	176	181	187
48	116	120	124	127	131	135	139	144	148	152	157	161	166	171	177	182	187
49	117	120	124	127	131	135	139	144	148	153	157	162	167	171	177	182	187
50	117	120	124	127	132	136	140	144	148	153	157	162	167	172	177	182	188
51	117	120	124	128	132	136	140	145	149	153	158	162	167	172	178	182	188
52	117	121	125	128	132	136	140	145	149	153	158	162	167	172	178	183	188
53	117	121	125	128	132	136	140	145	149	154	158	163	168	172	178	183	188
54	118	121	125	128	132	136	140	145	149	154	158	163	168	173	178	183	188
55	118	121	125	128	132	136	140	145	149	154	158	163	168	173	178	183	188

Circumference of the Chest.—The chest measurement furnishes a very good idea of the state of development. It is used in many countries in examining army recruits. Frölich[1] recommends the following method: The measuring tape is to be applied horizontally at the level of the nipples in front and just beneath the angles of the scapulæ behind while the arms are held horizontally. The measurements during extreme inspiration and again during extreme expiration are to be recorded, the difference representing the *chest expansion*. He found among recruits that the average in men of twenty years was for expiration 82 cm. ($32\frac{3}{4}$ in.), for inspiration 89 cm. ($35\frac{5}{8}$ in.), and the chest expansion 7 cm. ($2\frac{3}{4}$ in.), and he attaches considerable diagnostic importance to these figures, because he noted that in emphysema, in pulmonary consolidation, and pleural effusions the circumference, especially during expiration, was increased, while the chest expansion was diminished, and this diminution might persist for some time after

[1] H. Frölich, Die Brustmessung im Dienste der Medicin, Leipzig, 1894. A full bibliography is quoted here.

WEIGHT TABLE (FEMALE)

Age.	57 Ins.	58 Ins.	59 Ins.	60 Ins.	61 Ins.	62 Ins.	63 Ins.	64 Ins.	65 Ins.	66 Ins.	67 Ins.	68 Ins.	69 Ins.	70 Ins.	71 Ins.	72 Ins.	73 Ins.
20	100	103	106	109	113	116	120	123	127	130	134	138	142	147	152	156	161
21	101	104	107	110	114	117	120	124	127	131	135	139	143	148	152	157	162
22	101	105	107	110	114	118	121	124	128	132	136	140	144	149	153	158	162
23	102	105	108	111	115	118	122	125	128	132	137	140	145	149	154	158	163
24	102	106	108	111	115	119	122	126	129	133	137	141	145	150	155	159	164
25	103	106	109	112	116	119	123	126	130	134	138	142	146	151	155	160	165
26	103	107	110	113	117	120	124	127	131	134	139	143	147	151	156	161	166
27	104	107	110	113	117	121	124	128	131	135	139	144	148	152	157	162	166
28	104	108	111	114	118	121	125	128	132	136	140	144	149	153	158	162	167
29	105	108	111	114	118	122	126	129	133	136	141	145	149	154	158	163	168
30	105	109	112	115	119	123	126	129	133	137	141	146	150	154	159	164	169
31	106	109	112	116	119	123	127	130	134	138	142	146	151	155	160	165	170
32	106	110	113	116	120	124	127	131	135	138	143	147	151	156	161	166	170
33	107	110	113	117	120	124	128	131	135	139	143	148	152	156	162	166	171
34	107	110	114	117	121	125	128	132	136	140	144	149	153	157	162	167	172
35	108	111	115	118	122	125	129	133	137	140	145	150	154	158	163	168	173
36	108	112	115	119	122	126	130	133	137	141	146	150	154	159	164	169	174
37	109	112	116	119	123	126	130	134	138	142	146	151	155	160	165	170	175
38	109	113	116	120	123	127	131	135	139	142	147	152	156	161	166	170	175
39	110	113	117	120	124	128	131	135	139	143	148	153	157	161	166	171	176
40	110	114	117	121	124	128	132	135	140	144	148	153	157	162	167	172	177
41	111	114	118	121	125	129	132	136	140	145	149	154	158	163	168	173	178
42	111	115	118	122	125	129	133	137	141	145	150	155	159	163	169	173	179
43	112	115	119	122	126	130	134	138	142	146	150	156	159	164	169	174	179
44	112	116	119	123	127	130	134	138	142	147	151	156	160	165	170	175	180
45	113	116	120	123	127	131	135	139	143	147	152	157	161	166	171	175	181
46	113	117	120	124	128	131	136	139	143	148	152	157	162	166	171	176	182
47	114	117	121	124	128	132	136	140	144	149	153	158	162	167	172	177	182
48	114	118	121	125	129	133	137	141	144	149	154	159	163	168	173	178	183
49	115	118	122	125	129	133	138	141	145	150	154	159	164	168	174	179	184
50	115	119	122	126	130	134	138	142	146	150	155	160	164	169	174	179	185
51	116	119	123	126	130	134	139	143	147	151	156	161	165	170	175	180	186
52	116	120	123	127	131	135	139	143	147	152	156	161	166	170	176	181	186
53	117	120	124	127	131	135	140	144	148	153	157	162	166	171	177	182	187
54	117	120	124	128	132	136	140	144	148	153	158	162	167	172	177	182	188
55	118	121	125	128	132	136	140	145	149	154	158	163	168	173	178	183	188

the disease had subsided. The chest expansion is diminished (the so-called Bryson's sign) if the cartilages become ossified. This is often the case in exophthalmic goiter.

CONFIGURATION OF THE THORAX

NORMAL SHAPE OF THE CHEST

A normal chest, such as one sees so beautifully illustrated in the masterpieces of classic statuary, should be symmetric, the surface well rounded, without sharp corners or depressions; the intercostal spaces only visible between the lower ribs; the subcostal angle about 90°; the sternum nearly straight in profile, without a decided angle between the gladiolus and the manubrium; and the sternovertebral somewhat shorter than the transverse diameter. The gradual increase in the horizontal diameters of the thorax should form a sort of pyramid, with its base below, but the graduation should not be too marked, and the shoulder girdle, or in females the breast, should offset this difference. The shoulders should be nearly horizontal, the scapulæ lying flat against the back, clavicles not too prominent, and the supra- and infraspinous fossæ not too deep.

PATHOLOGIC SHAPES

Emphysematous Chests.—These abnormal forms depend upon an emphysematous enlargement of the lungs, and they possess one feature in common—the thorax seems abnormally widened and prominent. The sagittal diameter is generally increased and the subcostal angle more obtuse than in the normal thorax. When the emphysema is diffused over the entire lung or when mostly limited to the lower chest, the thorax looks as if in a normal position of deep inspiration; but when caused by forced expiration (coughing), the emphysema is situated more in the upper chest, because the respiratory power acts more upon the lower parts of the thorax. Then the upper thoracic aperture appears enlarged and the so-called "barrel chest" is produced. These are the two different types.

Fig. 5.—Emphysematous chest (Dr. W. H. Smith, Massachusetts General Hospital).

The Paralytic Thorax.—Contrasted with the emphysematous thorax, the so-called *paralytic thorax* is abnormally flat,[1] long, and sometimes narrow; the ribs, both in front and behind, have a marked downward direction; the intercostal spaces are widened; the subcostal angle

[1] [Woods Hutchinson, Niles, and others do not believe that the tuberculous chest is abnormally flat. The former (Jour. Amer. Med. Assoc., 1897, xxix, p. 512; ibid., 1903, xl, p. 1196) measured 20 tuberculous chests and found them to be more nearly round than the average normal chest. The measurements were made on an imaginary horizontal plane passing through the junction of the fourth costal cartilages with the sternum. Dividing the anteroposterior by the transverse diameter gives the ratio (usually expressed as a percentage) which

is very acute; the supra- and infraclavicular fossæ are deep; the intercostal muscles and those of the shoulder girdle are slightly developed; and the shoulder-blades project noticeably, like wings, because of a weakness of the muscles, especially of the serratus magnus. This type of chest is observed in *weakly* or *cachectic* individuals, and very commonly

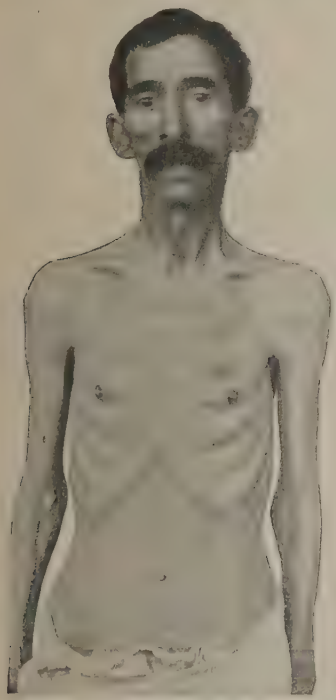


Fig. 6.—Paralytic chest (phthisis) (Dr. W. H. Smith, Massachusetts General Hospital).

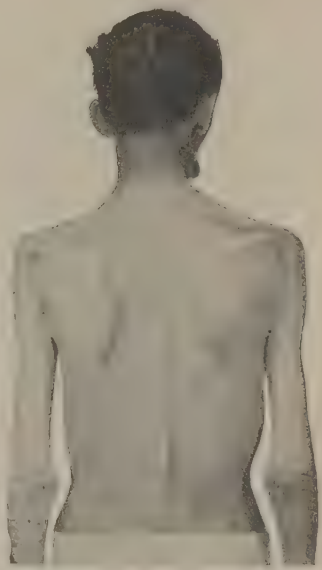


Fig. 7.—Paralytic chest (phthisis) (Dr. W. H. Smith, Massachusetts General Hospital).

in *phthisis*. It was formerly considered a predisposing cause of consumption, and is now frequently spoken of as "the phthisic chest."

The reader may consult D. Rothschild's original articles[1] for his views upon the importance of the so-called sternal angle, the angle between the manubrium and the body of the sternum, in the development of the paralytic thorax.

the former bears to the latter, and is called the *clinical index* of the chest. From several thousand measurements made in the German Army and at the Yale gymnasium the average normal adult clinical index is estimated at 70 per cent.; 350 cases of tuberculosis collected from various observers showed an average index of 79.7 per cent. Niles[2] found in 1022 measurements of tuberculous patients (about half of which he made himself) that 720 of them (70 per cent.) showed an index above 72 per cent., 219 (21 per cent.) of them were within normal limits, *i. e.*, between 68 and 72 per cent., while only 83 (8 per cent.) were below 68 per cent.—Ed.]

[1] Verhandl. d. Congresses f. innere Med., 1899, p. 590; and the monograph, Der Sternalwinkel, Frankfurt, J. Abt, 1900.

[2] Ibid., 1909, lii, p. 1916.

Scoliotic, Kyphotic, and Scoliokyphotic Thoraces.—These terms are applied to twists and deformities of the chest which are observed as a sequence of spinal curvature. They are frequently quite pronounced. It is often difficult to detect such deformities from the front; but by noting the low stature, the short thorax, and the marked breadth of shoulders an experienced eye can generally discover them.

Rachitic Chests.—Rickets may be responsible for all sorts of chest deformities. Perhaps the most characteristic is the keel-shaped prominence of the sternum called *pectus carinatum* (pigeon-breast). It is associated with a shortening of the anterior diagonal horizontal diameter and an increase in the sternovertebral diameter of the chest (Figs. 8, 9).

Fig. 8.—Pigeon-breast (Dr. R. C. Cabot, Massachusetts General Hospital).

A transverse groove (Harrison's groove) often marks the insertion of the diaphragm to the ribs. The so-called "rachitic rosary," a beaded enlargement at the line of junction of the bony ribs with their costal cartilages, can be felt as well as seen. It generally disappears in later childhood. The other rachitic deformities may persist, or they may become modified to a greater or less extent.

Boat-shaped Chest of Syringomyelia.—Pierre Marie and Astié [1] described, under the name of "thorax en bateau," a depression of the upper portion of the anterior chest-wall, which, so far as we know, is only observed in syringomyelia. The cavity lies in the median

[1] Soc. méd. des hôpitaux, 1897, 19, ii.

line, as if sunk against the spinal column, and extends downward as far as the lower edge of the pectoralis major; it may be as deep as 5 cm. The atrophy of the pectorals and of the other muscles takes no part in producing this appearance.

Funnel-shaped Chest and Cobbler's Chest.—The true *funnel-shaped chest* is either congenital or else develops gradually and without any known cause. It consists of a funnel-shaped depression of the lower end of the sternum, which frequently reaches quite deeply into the interior of the chest. It may lead to circulatory or respiratory disturbances resembling those observed in kyphoscoliosis. Cobblers

Fig. 9.—Rickets: Note the size and shape of head (see p. 37), the rosary, Harrison's groove, kyphosis, prominent belly, bowing of legs, and the enlargement of wrists (Dr. W. L. Stowell, Randall's Island Hospital).

may acquire a very similar deformity, due to the constant pressure against the lower end of the sternum. The cobbler type is, however, limited to the inferior portion of the sternum, or even to the xiphoid process alone.

Asymmetry of the Chest Due to Disease of the Thoracic or Abdominal Viscera.—An expansion or a contraction of one chest-half may result from various affections of the thoracic viscera, *e. g.*, a large pleural exudate, a pneumothorax, or even to a slight extent a croupous pneumonia. The alteration may be general over one entire side or localized. The affected side may be the larger or the smaller.

A considerable pleural effusion or a pneumothorax produces an enlargement of the affected side of the thorax, an obliteration of the intercostal spaces, a dislocation outward of the nipple and of the scapula, a convexity of the spine toward the affected side, and an elevation of that shoulder. The last two deformities, both probably due to an alteration of the center of gravity, make the patient look as if he were carrying a weight on the affected side.

The lower thorax may be enlarged by a decided increase in the size of the liver or spleen. Such an enlargement will become still more noticeable if tympanites or ascitic fluid distend the abdomen enough to prevent the dropping of the enlarged liver or spleen. An aortic aneurysm or an intrathoracic tumor may cause a localized enlargement of the thorax. This will be situated at the point of contact of the

Fig. 10.—Funnel-shaped chest (Dr. R. C. Cabot, Massachusetts General Hospital).

growth with the thoracic wall. Actual contact is not, however, necessary, because, even when the growth or aneurysm is merely in close proximity to the wall, a localized bulging will be caused by the diminution in the intrathoracic negative pressure, *e. g.*, an aortic aneurysm, even when covered by the lung, will cause a local prominence. Neither does a pleural effusion need to be under positive pressure, as is so commonly supposed, in order to enlarge the affected side of the chest. (See what is said regarding dislocation of organs by exudates, p. 87.) Cardiac enlargements and pericardial effusions give rise to a precordial bulging. The lower thorax will be quite uniformly and decidedly expanded by any marked increase in the contents of the abdomen, *e. g.*, meteorism, ascites, large ovarian tumors, or pancreatic cysts.

Chronic indurative processes in the lung, *e. g.*, chronic pneumonia with or without bronchiectasis, chronic tuberculosis, are apt to cause a

unilateral contraction of the thorax, sometimes including the entire half of the chest. The coincident pleuritic contraction may be partly responsible for the deformity. After the absorption of a pleuritic effusion it is very common to find a retraction of the affected side of the chest instead of the previous enlargement. This is due to the fact that the lung, incased in thick fibrous adhesions, has been compressed so long that it can never again expand fully, and that the pleuritic adhesions

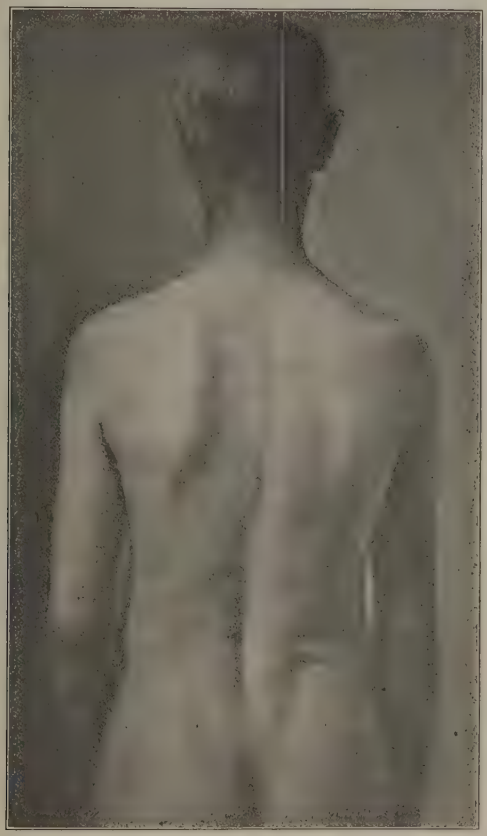


Fig. 11.—Scoliosis and asymmetry of the thorax: patient with fibroid phthisis of left lung; left chest smaller than right: left shoulder (affected side) higher than right; left scapula nearer the spine; dorsal spine concave to left; lumbar spine with a compensatory convexity to left (New York City Hospital).

tend to contract and draw the thorax in. These pulmonary and pleuritic conditions are, of course, very commonly combined. When the contraction of one side of the chest is very decided, the scapula, clavicle, and the neighboring soft parts are plainly depressed; the nipple and the shoulder then approach the median line, and the spinal column presents a curvature with a concavity toward the affected side. The corresponding dislocations of the thoracic viscera will be discussed under

Topographic Percussion. Noticeable increase in the depth of the supra- or infraclavicular fossæ suggests a retraction of the apices, and is, therefore, especially if unilateral, an early and important sign in pulmonary tuberculosis. [A localized prominence above the clavicle may be due to a cervical rib.[1] The tumor is usually situated one or two finger-breadths above the clavicle, is hard, more or less rounded, and generally immovable. There may be another upon the opposite side. Palpation may, and *x*-ray examination certainly will, distinguish this condition. For an account of the symptoms referable to the circulation and to the nervous system see the comprehensive article by Keen, which contains a complete bibliography. Thrombosis of the left subclavian and jugular veins in one of my patients at the City Hospital produced a localized supraclavicular tumor which simulated an enlarged lymph-node.—Ed.]

Inspection reveals these chest deformities more accurately than direct measuring with the tape; probably because the eye notes differences not only in the size of the chest, but in the extent of the respiratory excursions. The latter are, of course, always diminished on the affected side. The extent of the respiratory excursion is the surest way to decide whether a given deformity is due to an enlargement of one side or a contraction of the other side. Another reason why measuring with the tape is apt to be inaccurate in pleuritic effusions is this. The lower end of the sternum is generally dislocated to the affected side, so that the middle line of the sternum forms an acute angle with the true median line of the body. Therefore, measuring from the middle of the spinal column to the middle of the sternum is not accurate. We should measure to a plumb line dropped from the middle of the jugulum (ligne du cordon).

Woillez's cyrtometer is a practical instrument for measuring and picturing chest deformities, and is rather better than the ordinary tape; but, as a matter of fact, a narrow lead band, about the thickness of a lead pencil, is more convenient than the specially devised instrument. It can be accurately applied to the chest-wall at any desired level and removed without altering its shape; a tracing can then be made upon paper and measurements taken. In those cases in which the lead band cannot be removed without changing its shape the outline of the thorax should be obtained by taking the segments separately and allowing them to overlap. Such tracings are sometimes very instructive in following the course of an obstinate pleurisy. (For the discussion of more complicated apparatus see references cited below [2])

Rothschild employs the so-called sternogoniometer for the measurement of the sternal angle.[3]

SIZE AND SHAPE OF THE HEAD

According to Strümpell, the horizontal circumference of the skull in the newborn is normally 40 cm., at the end of the first year 45 cm., and at puberty 50 cm.

During the first eight or nine months the large fontanel slightly increases in size; about the tenth month it begins to diminish, and at the sixteenth month it should be closed.

Hydrocephalus may be either congenital or acquired early in life The skull is enlarged (up to 50 cm. in the first months of life), and most of the bones are separated by broad sutures and fontanels The cranium looks like a big bladder, tapering downward. The orbital roofs are projected downward, causing the eyes to look downward in a very characteristic fashion; and the face is diminutive in comparison. The cranial bones are very thin, and when pressed upon crackle like parchment

[1] W. W. Keen, Amer. Jour. Med. Sci., Feb., 1907, vol. cxxxiii, No. 2, p. 173.

[2] F. Schenk, "Zur Aetiologie der Skoliose," Vortrag, gehalten in der Chir. Section der 58, Versammlung deutscher Naturforscher und Aerzte zu Strassburg i. E. Berlin. Verlag von H. Heinicke. C. Hübscher, "Redresseur und Messapparat. Ein Beitrag zur Therapie der fixierten Skoliose," Beiträge zur klin. Chir., redigiert von P. Bruns, vol. xiii, part 1

[3] Verhandl. d. Congresses f. innere Med., 1899, p. 590; and the monograph, Der Sternalwinkel, Frankfurt, J. Abt, 1900.

Rachitis is characterized by a peculiar malformation of the skull. Although the longitudinal and transverse diameters are approximately normal, the cranium has a distinctive appearance, due to the prominent frontal and parietal eminences and to the flattened and vertical position of the occipital bone, forming the *square-shaped head* (tête carrée). The large fontanel may remain patent into the third, fourth, or even the sixth year, and the sutures a correspondingly long time. The

Fig. 12.—Hydrocephalus: Note size and shape of the head as compared with the face; the prominence of eyes and overhanging orbital roof; marked talipes equinovalgus of left foot (Dr. W. L. Stowell, Randall's Island Hospital).

thinned areas of bone over the cranium, and especially over the occipital bone, will furnish the same parchment crackling described above.[1]

[1] Special Pathology must be consulted for a description of the deformities of the face in acromegaly and of the asymmetry in hemiatrophia facialis progressiva.

EXAMINATION OF THE SKIN

An examination of the skin should not be restricted to cutaneous diseases alone, because in diseases of the internal organs we meet with all manner of changes in the skin, which can be appreciated by the sense of sight or by that of touch.

COLOR OF THE SKIN

The normal fleshy tint of the skin is due to the color of the blood shining through the epidermis and the superficial layers of the cuticle. The color of the skin may be modified, both physiologically and pathologically, by (1) a quantitative increase or decrease in the amount of flesh color; (2) a qualitative change due to abnormal pigmentation. The first is better observed in the face; the second, in other parts of the body, where the normal flesh color is not so prominent. Many qualitative variations, occasioned by abnormal pigmentation, are, however, determined better over paler uncovered areas.

QUANTITATIVE CHANGES OF THE FLESH COLOR

The intensity of the flesh color depends upon—(1) the intensity of the blood color; (2) upon the amount of blood contained in the vessels; (3) upon the thickness of the layers of skin covering the vessels. Any one of these three factors may vary and so cause alterations in the flesh color of more or less diagnostic importance.

PALLOR

Pallor Depending Upon Oligochromemia.—A pale face presupposes anemia, or a diminution of the coloring power of the blood (oligochromemia)—that is to say, a qualitative alteration of the blood. For we do not recognize any real quantitative diminution ("blood poverty" of the Germans) except that which occurs after a profuse hemorrhage, and this is rapidly made up by reabsorption of lymph and water, thus causing again the condition of oligochromemia. As we shall see later on, pallor is a very uncertain guide in the diagnosis of oligochromemia.

Pallor without Oligochromemia.—It is impossible to diagnose anemia from pallor alone. A careful blood-examination (see Section on p. 765) is absolutely essential in order to avoid the mistake of diagnosing anemia in a patient with normal blood simply because his face is pale; or reassuring a patient with red cheeks whose hemoglobin percentage is only 50.

Aside from oligochromemia, the causes of pallor of the face are numerous, *e. g.*, many people absolutely well, without a symptom or sign of disease, are abnormally pale. The only way to explain such pallor, providing, of course, the conjunctival and mucous membranes are not so pale, is to assume either an abnormal opacity of the epidermis or a scanty supply of blood-vessels in the face. During the course of an illness a patient sometimes gradually becomes paler and paler, and although the hemoglobin percentage remains normal, the physician, unless he examines the blood, will certainly consider the condition

one of oligochromemia. Here we must suppose that the pallor is due either to a diminution of the total amount of blood, or that the skin contains less blood than normally as a result of morbid changes in the circulation. We are usually unable to determine clinically which of these two factors is responsible for the pallor, because we possess no simple, accurate, and practical method of determining the amount of blood in the living body, and because we know very little regarding the diminution of the quantity of blood in relation to the body weight except in cases of hemorrhage.[1] That altered circulatory conditions do occur in many cases of morbid pallor is made all the more probable by the existence of certain other symptoms,—weakness of the pulse, general bodily weakness, slight grade of cyanosis (see p. 40, et seq.), dilatation of the external cutaneous veins, nausea, dizziness,—such as are frequently observed from a diminished arterial blood-supply to the brain. It is difficult to determine whether the diminished amount of blood in the small arteries and capillaries, which is certainly the cause of the pallor, depends upon an alteration in the cardiac activity or in the capillary tonus. Pallor is associated with a low blood-pressure if entirely dependent upon diminished cardiac activity, the capillary tonus remaining constant; but if the small arteries dilate, pallor does not result. High blood-pressure is characterized by a marked pallor, provided there is a very decided capillary tonus.

A closer study of the connection between a normal hemoglobin percentage and this pallor would be of some service for careful treatment; because so long as every pale patient is considered anemic, as is, unfortunately, too often the case in practice, we shall not progress very far toward proper therapy. Affections of the stomach, heart disease, phthisis, and cachexias of all kinds, although associated with pallor, often show a normal blood. All such conditions may, of course, lead later on to oligochromemia.

The temporary pallor caused by nausea, collapse, or violent psychic impressions practically comes under the head of an alteration in circulation, being due partly to vasomotor influences but partly to cardiac weakness inducing lowered arterial pressure.

ABNORMAL REDNESS OF THE SKIN OF THE FACE

If the above conditions which produce pallor be reversed, an abnormal redness of the skin will result. A hemoglobin percentage as high as 120, although very rare, may be responsible for an increased color. The actual existence of such a condition as true plethora is uncertain because of the lack of any simple method for the determination of the quantity of the blood in the organism. Nevertheless, true plethora probably does exist, not only in the diseases recently described, as polycythemia, but also in such ruddy individuals as have always been designated by the laity as full-blooded. The grounds of probability furnished by v. Recklinghausen for the existence of true plethora in this latter group seem to have been thoroughly justified. In many cases such an appearance is caused by an abnormally thin or transparent skin; in

[1] Although it seems probable that extreme emaciation is associated with a diminution in the amount of blood, it has never been proved that this diminution is out of proportion to the loss of body weight. See also section upon "The Determination of the Quantity of the Blood."

others, by a local increase in the amount of blood sent to the face. The so-called "rosy chlorotics" are supposed to possess blood-vessels of abnormal transparency. In all such cases an examination of the blood is absolutely essential before a diagnosis of oligochromemia can be made. A suggestion is, however, often obtained by comparing the pallor of the conjunctivæ with the rosy hue of the cheeks.

People who spend most of the day out-of-doors, and especially those who are exposed to all sorts of weather, generally acquire a ruddy face from the constant increase of blood in the exposed portions.

Alcoholics are usually flushed on account of the dilating influence of alcohol upon the vessels. Minute dilated radicles may also be seen just underneath the epidermis, or an acne rosacea, which is so frequent in drinkers. As is well known, this same peculiarity is often observed in perfectly healthy individuals, in whom it is difficult to determine any cause. Fever produces a characteristic redness, ordinarily combined with some puffiness and moisture of the skin of the face. The lax condition of the muscular coat of the vessels is apparently responsible. This is evident in a sphygmographic tracing. The flush of fever is most noticeable in the cheeks, especially when contrasted with a pallor such as is observed in tuberculous patients (so-called hectic flush). Psychic excitement, shame, violent physical exertion, external applications of heat to the skin (baths, insolation), the inhalation of nitrite of amyl, or a moderate grade of atropin- or opium-poisoning, all cause a flushing of the face from vasomotor influences. The reddening in these cases may spread to the neck and to the upper part of the trunk. Poisoning with carbon monoxid ordinarily produces a very intense redness of the face, which is supposed to be due to an alteration of the blood. The latter, however, contains so little carbon monoxid that it is even difficult to determine it with the spectroscope, so that the explanation is unsatisfactory.

Hemicrania and some affections of the cervical sympathetic sometimes cause a unilateral redness of the face, which is commonly associated with a unilateral pupillary change. The redness of the face associated with various cutaneous diseases and the acute exanthemata need not be discussed.

CYANOSIS

By this term is meant a bluish tinge of the skin and mucous membranes which depends upon the poverty of the capillary blood in oxygen and its abnormal richness in carbon dioxid. The cutaneous capillaries may be either of normal or dilated caliber. In the former instance we have the so-called pale cyanosis; in the latter, the dark cyanosis. Since it is even a deeper blue than ordinary venous blood, we must assume in explanation some peculiarity in the skin-covering.

General Cyanosis.—A number of factors share in the production of general cyanosis:

(1) Insufficient oxidation of the blood in the lungs from any cause, so that the arterial blood in the capillaries is poor in oxygen and therefore dark.

(2) Cardiac obstruction to the venous return, so that the veins are dilated, the skin contains more venous blood than normally, the current is sluggish, and the blood is charged with more carbonic acid.

(3) Combination of (1) and (2).

(4) Vasomotor dilatation of the cutaneous capillaries (vasomotor paralysis), with a coincident disturbance of the general interchange of gases.

In (1) we have a pale, in (2) to (4) a more or less dark, cyanosis.

When due to cardiac obstruction, the most intense cyanosis is observed in the extremities because the circulatory difficulty increases with the distance from the heart; but the intensity of the cyanosis may also be affected locally by vasomotor influences. The face, especially the cheeks, lips, and ears, shows cyanosis very plainly because the color of the blood is more apparent in these situations even in health. The marked cyanosis which is sometimes observed in the nose and in the knees is to be attributed to vasomotor influences.

General cyanosis will therefore appear in any respiratory or circulatory affection. These two systems are so intimately related and so dependent one upon the other that if the cyanosis be very pronounced, we should naturally attribute it to an interference with both respiration and circulation, no matter which is primarily affected.

The following disturbances, primarily *respiratory*, cause cyanosis: Any affection preventing the free entrance of air to the lungs, *e. g.*, retropharyngeal abscess; croup; pseudocroup; edema or spasm of the glottis; paralysis of the inferior laryngeal nerve; tumor of the larynx; foreign bodies in the pharynx, larynx, trachea, or bronchi; any kind of tracheal stenosis, as by goiter or other tumors; strangulation; bronchitis; bronchial asthma, etc.

Affections which diminish the amount of breathing surface of the lungs, *e. g.*, emphysema; all varieties of pulmonary infiltration; atelectasis; compression of the lungs by an exudation or by pneumothorax. In this connection it is interesting to note that in pulmonary consumption the cyanosis does not reach so high a grade as the amount of breathing surface involved would lead us to expect. This is probably because the emaciated body contains less blood and needs less oxygen, so that what remains of the healthy lung tissue is practically sufficient to aërate the diminished amount of blood.

All affections which influence the activity of the respiratory muscles: paralyses and atrophies of the muscles of respiration (bulbar paralysis, etc.), as well as spasms (tetanus, epilepsy); further, any affection causing pain enough to inhibit respiration.

In all these disturbances the arterialization of the blood in the lungs is primarily affected, and later on some venous congestion is apt to result because the circulation lacks the help of the pumping action of respiration.

The following disturbances, primarily *circulatory*, cause cyanosis from congestion:

Uncompensated cardiac affections; valvular lesions and affections of the heart muscle; arteriosclerotic, cardiac, and nephritic changes; strains upon the heart; pericarditis, etc., as well as paralysis of the vasomotors.

Mitral defects, both those of insufficiency and those of stenosis, even when compensated, cause a certain degree of cyanosis. This is respiratory in nature, and depends upon the increased pressure in the pulmonary circulation, upon the resulting rigidity and brown induration of the lungs, and upon the accompanying bronchial catarrh, all of which impede the respiration.

The cyanosis of *congenital heart disease* is often more pronounced than

in any other condition. It depends upon venous congestion, or upon the admixture of arterial with venous blood, or upon both. This admixture is not, however, the only cause of the often enormous cyanosis presented by these cases. (See section upon Congenital Heart Lesions.)

The cyanosis which is caused by *vasomotor paralysis* depends upon a dilatation of the small vessels (the arterioles, capillaries, and smallest veins). It differs from the other types of general cyanosis in a lack of distention of the larger veins, and in the peculiar grayish-blue color of the entire surface of the body, without the localization at certain points of predilection, which is so characteristic of the other forms. (See the following section.)

Certain poisons, notably antifebrin and nitrobenzol, turn the blood very dark by changing the hemoglobin into methemoglobin. This is not a true cyanosis, although the body surface is blue.

Cyanosis from Local Causes.—Localized areas of the skin may become cyanotic without any disturbance of the general circulatory or respiratory system. Either local venous congestion from compression or thrombosis of large or small veins, or else some vasomotor disturbance, will be found to be responsible. Examples of the latter variety are the cyanosis of the hands, feet, and ears produced by the local action of cold, the cyanosis of paralyzed extremities, of the hands and feet of hysteric individuals, and occasionally of perfectly healthy individuals. In many patients this local cyanosis is not infrequently combined with an edema of the affected part; and it has been claimed, although upon insufficient grounds, that such a combination has some connection with hysteria (œdème bleu des hystériques, see p. 55).

This purely vasomotor cyanosis evidently depends upon a degree of vascular dilatation sufficient to produce stagnation from inadequate *vis à tergo*. The process may be compared to a running stream which, from the lack of a definite river-bed, becomes a swamp. One might think that such a dilatation of the vascular system, by diminishing the resistance, would assist the current. In this case, however, the current would not flow uniformly over so wide a territory, but through the shortest channels the current is very rapid, whereas the parts at some distance from these direct channels contain blood which is almost stagnant. The bright-scarlet spots which the writer has frequently observed scattered through the blue of vasomotor cyanosis furnish a proof of the accuracy of this theory. They correspond to areas of increased capillary current.

A cyanosis of similar origin appears in certain inflammatory processes. When extreme it is, of course, an unfavorable sign.

Cyanosis of the skin is naturally associated with increased loss of heat, so that cyanotic parts generally feel cold.

ICTERIC COLORATION OF THE SKIN (JAUNDICE)

Icterus is the peculiar pathologic yellow discoloration of the skin and mucous membranes, caused by bile-pigment or some of its derivatives. The ordinary form (*obstructive icterus*) depends upon a total or a partial occlusion of the bile-duct, so that instead of being emptied into the intestine, some or all of the bile is absorbed and stains the various tissues, *e. g.*, the skin and the mucous membranes. This discoloration varies in tint from a pale lemon yellow to a dark brown, olive green, or almost black. The darker shades (*melasicterus*) always signify an obstruction of long duration. They are caused either by a great excess of pigment accumulated in the skin or by a transformation of the original bile-pigment to related darker pigments.

Icterus is usually first noticed in the conjunctiva of the sclera and upon the unexposed parts, which are covered with but a thin layer of epidermis and are only slightly pigmented. After the obstruction has persisted for a short time the skin of the face and the mucous membrane of the mouth share in the discoloration. Pressure of the finger, by diminishing the amount of blood, sometimes makes the yellow of a mild icterus plainer. Because the gums are normally so pale they show icterus before the rest of the mouth-lining. Unless very intense, jaundice cannot be appreciated by artificial light.

In looking for icterus we generally begin by examining the conjunctivæ. We should remember that the yellowish color of the subconjunctival fat, so pronounced in cachectic individuals and in drunkards, is sometimes mistaken for icterus. The distribution of this fat is largely limited to the neighborhood of the folds in the mucous membrane, so that a careful examination of the tightly drawn conjunctiva nearer the cornea generally prevents a mistake. *Pingueculæ*, peculiar formations of colloid degenerated connective tissue which contain yellow pigment, are situated within the palpebral folds on either side of the cornea. They may be another source of confusion.

Certain races and some individuals exhibit a yellowish tint of skin, which a beginner might confuse with a faint jaundice; but a careful examination of the conjunctiva should prevent this mistake.

The yellowish discoloration in picric-acid poisoning can be easily differentiated from icterus by the history, etc., as well as by the urinary examination.

Bile-pigment occurs in the urine and sweat of icteric individuals. Yellowish stains upon the linen sometimes attract a patient's attention before he has observed the yellow color of his skin. The saliva is, for the most part, unaffected. The feces become pale and more or less clay-colored on account of the lack of bile. The absorption of certain biliary salts with the biliary pigment produces, at least in fresh cases, a slowing of the pulse and considerable itching of the skin.

Although obstructive jaundice arises most frequently from a catarrh of the biliary passages, it may depend upon serious changes in the liver itself, *e. g.*, cirrhosis, carcinoma, abscess.

Another type of jaundice which differs from the obstructive by the fact that the feces are unaffected (*i. e.*, of normal color) depends upon very imperfectly understood causes.

Icterus neonatorum belongs to this type. The old idea was that the drying up of the blood-current in the umbilical vein after birth caused a sufficient lowering of the pressure in the portal vein to enable the bile-pigment to pass from the liver into the portal vein. Quincke[1] and Schreiber[2] defend Peter Frank's theory of the cause of jaundice in the newborn. Frank argued that the bilirubin absorbed from the meconium, instead of being stored up in the liver for further use, escapes directly into the general circulation by way of the ductus venosus Arantii. This duct generally remains open for a short time after birth. One argument in favor of this theory is the fact that icterus neonatorum occurs most frequently in premature infants.

The cause of the jaundice which is not infrequently observed in infectious diseases (pneumonia, pyemia, and yellow fever) is not perfectly clear; it probably depends upon the absorption of bile-pigment from the liver. It has been claimed that a catarrh of the biliary passages, due to the general venous congestion, is responsible for the jaundice in pneumonia, but microscopic examinations of the liver tissues in such cases have shown that the bile-ducts were normal. Stagnation and reabsorption of bile from the lack of the usual rhythmic pressure exerted by the diaphragm upon the liver has been cited as another explanation of the icterus in pneumonia. If jaundice occurred only with pneumonia which involved the lower right lobe, this theory might seem more plausible. Experience in acute yellow atrophy of the liver has shown that under some circumstances a parenchymatous degeneration of the liver without any biliary obstruction may be the cause of a

[1] Arch. f. exp. Path., vol. xix, p. 34 et seq. [2] Berlin. klin. Woch., 1895, No. 25.

reabsorption icterus, so that it does not seem impossible that a similar process, of which more will be said later, may be the cause of the icterus in pneumonia, pyemia, and yellow fever. Liebermeister created an expression to embody this idea in the term "acatectic" icterus (κατέχειν, to hold back) or *diffusion icterus*.

The term *hematogenous icterus* was formerly applied to all these cases of obscure jaundice as well as to that found after poisoning by ether, chloral, chloroform, potassium chlorid, arsenic trioxid, or toluylendiamin. It was assumed that the biliary or other pigment was formed in the circulatory system from the coloring-matter of the blood, more especially because most of these poisons are capable of destroying the red corpuscles. More accurate experiments in the poisoning of arsenic trioxid and toluylendiamin have proved that the yellow pigment is formed from an alteration of the hemoglobin of the red corpuscles into bile-pigment; but within the liver, not in the blood itself. This excessive accumulation of biliary pigment can be demonstrated microscopically in the capillary bile-ducts, and a part of it passes into the circulation by a process which will subsequently be described. Again, it was shown that in some cases of poisoning the destruction of red corpuscles was so extensive that the liver was incapable of altering all the hemoglobin to bile-pigment, so that a part of it had to be eliminated as such in the urine. These results explain the connection so frequently observed between other varieties of hemoglobinuria and the frequent combination with icterus. It is therefore advisable to distinguish from the *diffusion icterus* described above all such cases of hematohepatogenous or pleiochromic icterus, and to include under the latter term only those in which we can demonstrate a destruction of the red corpuscles, or a hemoglobinuria.

This modern conception of hematohepatogenous jaundice has obviated the necessity which formerly existed of distinguishing between hematogenous and hepatogenous jaundice by the presence of biliary acids in the latter and their absence in the former. Such a distinction was, however, unnecessary, because cases of obstructive jaundice sometimes present no biliary acids in the urine, and, besides, biliary acids are sometimes found in perfectly healthy individuals.

Géraudel's investigations[1] have markedly clarified our views upon the pathogenesis of icterus. From anatomic investigations of the liver in obstructive jaundice, in which only the periphery of the acinus was preserved, the central portion having degenerated, this writer came to the conclusion that the liver actually consists of two glands, structurally combined but functionally distinct: the portal gland (the periphery of the acinus) and the subhepatic gland (the center of the acinus). The periphery of the acinus produces the biliary constituents, particularly the biliary pigment, and throws them back into the liver blood-stream. The capillary blood-vessels of the liver carry these specific biliary constituents to the subhepatic gland (the center of the acinus), which eliminates them through the biliary passages. The secretion of the biliary constituents into the blood in obstructive jaundice corresponds in a measure to the first step of the physiologic process of bile-formation. Icterus appears because the second step, the elimination by the subhepatic gland, has been interrupted by the closure of the secretory ducts. The writer considers plausible the supposition that the acatectic or diffusion icterus (in acute yellow atrophy of the liver, for example) depends entirely upon the fact that from some cause the eliminating function of the subhepatic gland has been interfered with, while the formation of biliary pigment by the portal gland has not been disturbed. Géraudel's theory also furnishes a simple explanation for the hematohepatogenous or pleichromic icterus, since it is only necessary to assume that the subhepatic gland is unable to eliminate the biliary pigments which are formed in excessive quantities by the portal gland and secreted into the capillary blood-stream. With such a conception the insufficient elimination is readily understood, whereas if we follow the old theory and ascribe the production and the elimination of the biliary pigments to the same cells, it is hard to see why the biliary pigments are not eliminated as well as produced.

So far we have assumed that the pigmentation which occasions jaundice is real bile-pigment, *i. e.*, *bilirubin*. In most cases this supposition cannot be questioned, for bilirubin can be demonstrated in the urine. But there are numerous other cases in which only *urobilin* (hydrobilirubin) can be found. The latter have been designated as *urobilin icterus*, *i. e.*, icterus due to the deposition of the urobilin in the

[1] Jour. de Physiol., vol. viii, part 1, pp. 69 and 103.

skin. But it is probable that such an assumption is arbitrary because the bilirubin in the tissues may be excreted in the urine as bilirubin: for, in the first place, urobilin possesses a very much slighter coloring power than bilirubin; in the second place, the serum in cases of urobilin icterus always contains bilirubin; in the third place, an enormous amount of urobilin may be found in the urine without a trace of jaundice; and, finally, Leube has demonstrated bilirubin in the sweat of patients with so-called urobilin icterus. The term should, therefore, imply merely that urobilin alone is excreted in the urine, whereas the supposition that the yellowish discoloration of the skin is due to urobilin is probably erroneous. Such a type of icterus is generally of a very mild grade. It is observed especially in cirrhosis of the liver and during the subsidence of ordinary obstructive icterus.

ABNORMAL PIGMENTATION OF THE SKIN

Pigmentation of the skin, as is well known, varies a great deal within physiologic limits. It is most pronounced in brunettes, and more marked upon the exposed body parts of any one, *e. g.*, face and hands, as well as about the genitals and the anus, in the axillæ, on the nipples, and in the linea alba. During pregnancy the pigmentation is generally markedly increased about the areolæ of the nipples and in the linea alba, and, besides, areas of irregular mottling may appear upon the face or other body parts—the so-called "chloasma uterinum" (chloasma gravidarum, masque de la grossesse).

Ephelides or *freckles* can scarcely be called pathologic pigmentation. Their distribution upon the hands and face, especially in individuals with red hair, and their frequent disappearance during the winter, fall within physiologic limits and have no diagnostic importance.

Itching cutaneous diseases often leave behind a permanent pigmentation, due to the scratching. The characteristic arrangement of this pigmentation in streaks, as well as the history, always points to its origin. It is often decidedly marked between the shoulder-blades in individuals who have suffered from body lice, because these insects seem to have a preference for the folds of the shirt in this region. The so-called "*vagabond's disease*," sometimes presenting a very dark-brown color (due to serious and persistent infestation with all sorts of vermin and constant scratching, as well as to accumulation of dirt), might in rare instances be confused with Addison's disease.

Melanosarcoma, especially *melanosarcomatosis*, is accompanied by a diffuse gray to black discoloration of the skin and by the excretion of melanin in the urine. (See Examination of the Urine.)

Pulmonary tuberculosis is sometimes associated with a decided brownish coloration of the face or of the entire body. *Measles* occasionally leaves behind traces of its existence in the shape of brownish pigmented spots, whose form and arrangement are sufficiently characteristic for recognition. *Mustard plasters*, *blisters*, and *Baunscheidtismus* produce a localized pigmentation which is sometimes permanent.

Morbus Addisoni causes a smoky-gray to bronze discoloration of the skin, which is the most important diagnostic symptom. Other associated symptoms are: well-marked digestive disorders, *e. g.*, dyspepsia, vomiting, diarrhea; certain nervous symptoms; and a gradually increasing cachexia. The pigmentation usually appears first upon areas

where the pigment of the skin is normally intensified, such as the face, hands, axillæ; also wherever there is any friction upon the skin, such as the waist-line or around the neck. At first a pale, smoky-gray, the discoloration deepens to a bronze-brown, resembling the color of a mulatto, and tiny spots of an intense brown or even black color are observed scattered over this uniformly brown background. The mucous membranes are involved as well as the skin, and although not so commonly observed in the conjunctivæ, a few grayish patches upon the buccal mucosa, especially just inside the lips and cheeks, are rather characteristic of Addison's disease. In well-marked examples of this disease the only parts exempt from pigmentation are the palms of the hands, the soles of the feet, and the nails. To distinguish this affection from *melasicterus*, the urine should be tested for bile-pigment; it is invariably present in the latter. The mucous membranes of the mouth should also be examined for pigmentation spots; they are commonly present in the former. The patient's history and his general condition will clinch the diagnosis. The pigmentation which is occasionally observed in pulmonary tuberculosis may be a source of error, especially since patients afflicted with Addison's disease often suffer from pulmonary tuberculosis as well. The selection of the mucous membranes, the progressive nature of the pigmentation, as well as the entire symptom-complex in morbus Addisoni, usually facilitate a distinction. That the pigmentation observed in pulmonary tuberculosis is closely related to that of Addison's disease is evidenced not only by their similarity, but also by the fact that severe cases of pulmonary tuberculosis exhibit border-line symptoms with Addison's disease and almost constantly reveal histologic changes in the suprarenal bodies.

It is well to caution the reader that, although this pigmentation of the buccal mucous membranes is one of the most characteristic signs in morbus Addisoni, an identical appearance is sometimes observed in perfectly healthy brunettes, and particularly along with the pigmentations associated with diseases of the liver (see the following).

Hepatic cirrhosis and some of the other liver diseases occasionally exhibit a peculiar brownish discoloration of the skin, which differs from icterus in being rather more of a dirty-gray shade and somewhat spotted in arrangement. The absence of bile-pigment in the urine and of a yellowish tinge in the conjunctivæ will prevent any mistake. The cause of this pigmentation is as yet undetermined, but since the description of bronzed diabetes its occurrence has acquired a certain importance. Diabète bronzée, first described by the French, presents a combination of diabetes, hepatic cirrhosis, and pigmentation of the skin. In the cases observed by the author there was neither pigmentation of the mucous membranes nor any of the intense brownish-black spots of pigment so characteristic of Addison's disease, although both symptoms may be present in this affection. The presence of glucose in the urine, the demonstration of cirrhosis of the liver without icterus, and the lack of the characteristic symptom-complex of Addison's disease will ordinarily very readily determine a diagnosis.

The continued administration of silver or arsenic preparations is sometimes responsible for a dark pigmentation of the skin. *Argyria* depends upon the deposition of metallic silver, not only in the internal organs, but also in the skin and mucous membranes. It may look like

Addison's disease, but is not associated with any symptoms of illness. Besides, the nails are discolored as well as the rest of the integument. To-day silver nitrate is employed so little in the therapy of nervous diseases that this form of pigmentation is of very rare occurrence. *Arsenic melanosis* is very much more difficult to distinguish from Addison's disease, for the small dark spots scattered about in the diffuse pigmentation, the involvement of the mucous membranes of the mouth, and, in fact, all the peculiarities of Addison's disease have been observed to follow the persistent use of arsenic. The pigmentation itself seems to be derived from the blood-coloring matter. A further difficulty in differential diagnosis depends upon the fact that the arsenic has generally been employed for some cachectic condition, *e. g.*, pernicious anemia, so that the accompanying history will not always solve the difficulty. If the pigmentation diminishes after the arsenic has been stopped, as in a case observed by the author, the diagnosis could be made with probability. We must acknowledge, however, that even very small doses of arsenic sometimes cause arsenic melanosis and that stopping the drug does not always diminish the pigmentation.

[Thirteen cases of *ochronosis* (a total of 14) have been described since Virchow first named this very rare condition in 1866.[1] The light brown to deep black coloration depends upon a staining of the cartilages and fibrous tissues. This characteristic serves to distinguish it from the pigmentation of the skin itself just described in Addison's disease; although in one of the cases, Pope's,[2] the face showed a marked resemblance to this latter affection and an autopsy revealed disease of the suprarenal glands. The collection of color so characteristic of ochronosis[3] is a semilunar or V-shaped patch of brown to black, and is situated in the sclerotic coat just outside the edge of the cornea. The next most characteristic situation is the cavity of the antihelix. Here the coloration is more bluish or leaden black. Other situations are, the costal or any cartilages, the tendons of the wrists, and the fibrous tissue of the palms of the hands. Four of the reported cases had chronic arthritis, and Osler mentions the peculiar gait, "a curious waddle in walking," of 2 of the cases seen by him. In 9 cases the excretion of dark urine or of urine which became black on standing has been described as continuous or intermittent. Three of the cases have exhibited a definite carboluria, and 4 of them an alkaptonuria. The relationship between the latter and ochronosis was first suggested by Albrecht.—Ed.]

The reader is referred to text-books upon skin diseases for the consideration of the numerous cutaneous affections accompanied by pigmentation, *e. g.*, *nævus pigmentosus*, *lentigo*, *albinismus partialis* and *universalis*, *vitiligo*, and *peliosis*.

MOISTURE OF THE SKIN; SWEAT EXCRETION

An abnormally dry skin will be observed in any condition where the amount of water absorbed by the digestive organs is limited, or where a large amount of water is removed from the body in some other way than by means of the sweat-glands, *e. g.*, profuse diarrhea, excessive vomiting, digestive diseases with diminished absorption, diabetes mellitus and insipidus, chronic nephritis with polyuria, marked edema of the skin, etc. An increased production of sweat is observed in certain

[1] Virchow's Arch., 1866, vol. xxxvii, p. 212.

[2] [The Lancet, January 6, 1906, p. 24, contains a table of 11 cases and a colored illustration.—Ed.]

[3] [The fourteenth case is reported by Reid, Osler, and Garrod in the Quarterly Journal of Medicine, vol. i, No. 2, p. 199. An excellent colored plate accompanies their description.—Ed.]

fevers, especially in acute articular rheumatism, acute polyneuritis, and epidemic sudamina.

The excretion of sweat is one of nature's methods of cooling the body, under both physiologic and pathologic conditions. When the temperature in any febrile affection drops rapidly, whether spontaneously or under the influence of drugs, a profuse sweat usually accompanies the fall, *e. g.*, at the crisis of penumonia, at the drop of temperature in malaria, and during the third week of typhoid fever, when the temperature begins to remit. The hectic sweats of phthisis, which are so annoying and prognostically serious, coincide with the fall of temperature. They usually occur at night or in the early morning. In some patients, to be sure, they are independent of any fever and, like the increased pulse-rate, are merely a symptom of tuberculous intoxication. They are generally associated with a sense of considerable weakness,

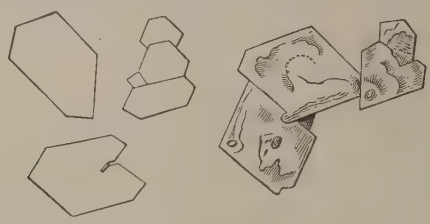


Fig. 13.—Crystals of nitrate and oxalate of urea obtained from deposits upon the skin (after Leube).

probably connected with the vascular relaxation from the loss of water, for copious draughts of water sometimes counteract them.

We may also mention the sweating produced by hot baths and hot drinks, by pilocarpin, by ammonium acetate, and by most antipyretic measures. Salvia, atropin, eumydrin, agaricin, camphoric acid, and sulphonal, on the contrary, check the sweat secretion.

In certain types of nephritis, interference in renal activity is associated with an increased production of sweat, and sometimes with the deposition of crystalline scales of urea upon the skin (Fig. 13), particularly of the face. To recognize these crystals, the deposit should be scraped off upon a glass slide, dissolved in dilute nitric or oxalic acid, and then allowed to evaporate. Crystals of sodium chlorid are often found instead of urea. As a general rule, especially with much edema, nephritic cases are associated with a diminution in the sweat production.

The sweat in jaundice may be colored yellow. In other conditions different colors have been noted, although not explained (chromidrosis). The most frequent is brownish-red sweat; its etiology is unknown. Blue sweat has been described, and is probably due to the growth of the Bacillus pyocyaneus in the skin. Naturally, variously colored underclothes may be a cause of coloring the sweat, especially since the use of anilin dyes has become so universal. Bloody sweat (hemidrosis) has undoubtedly been observed. It is exceedingly rare, however, and the conditions under which it occurs are obscure and by no means uniform.

SWELLING AND EDEMA OF THE CUTANEOUS AND SUBCUTANEOUS TISSUES

Swelling or turgidity of the skin depends upon an increase in the amount of fluid contained in its tissue, *i. e.*, of the blood and lymph. *Increased turgidity* accompanies plethora, fever, and all conditions associated with an increased supply of blood to the skin, or with circulatory excitement. *Diminished turgidity* accompanies all conditions associated with a diminished amount of fluid in the skin, *e. g.*, cachexia and an impoverishment of the general watery elements of the body. *Increased turgidity* presents an increased fulness, a rounded outline of the surface; it obliterates the lines, especially of the face, and is generally combined with a deepening of the fleshy tint. *Diminished turgidity* is characterized by sharper outlines of the parts and by pallor. With the poverty in fluid the skin loses some of its elasticity, and the wrinkles and lines of the face are emphasized.

Anasarca, general dropsy or *edema of the skin*, means the pathologic increase of fluid in the lymph-spaces and subcutaneous tissues. The difference between edema and turgidity is one of degree. Despite the increase of fluid, the elasticity of the skin is diminished in edema, as is evidenced not by the wrinkles, but by the so-called pitting of the skin on pressure.

Edema always indicates an obstruction to the flow of lymph, with some lack of proportion between its influx and exit, so that an equilibrium is obtained only after the high pressure has distended the meshes of the tissues.

According to Starling, the factors which coöperate, usually in manifold combinations, to produce cutaneous turgidity and edema are:

1. Factors which cause increased transudation:
   - (*A*) Increased capillary pressure from—
     - (*a*) Venous obstruction.
     - (*b*) Vasodilatation.[1]
     - (*c*) Plethora.
   - (*B*) Increased permeability of the capillary walls from—
     - (*a*) Local injury by mechanic, thermic, or chemic agencies.
     - (*b*) Nutritive disturbances of the capillary walls.
     - (*c*) General injury to the capillary walls by circulating poisons.
   - (*C*) A watery condition of the blood (hydremia).

2. Factors which cause diminished drainage or absorption of the fluid in the tissues.
   - (*A*) Disturbances of drainage through the lymphatic vessels due to—
     - (*a*) Paralysis of the extremities.
     - (*b*) Closure of the lymphatic trunks.
   - (*B*) Disturbances of absorption through the veins due to—
     - (*a*) Venous obstruction.
     - (*b*) A watery condition of the blood.
     - (*c*) A highly concentrated transudate.

As previously stated, to produce edema it is almost always necessary for several of these agencies to act together. The diminution of the elasticity of the tissues (Landerer) must also be mentioned as an additional factor.

Moreover, in addition to the purely physical and chemical factors, cited in the above scheme, which affect the permeability of the capillaries, we must also bear in

[1] In order that vasodilatation should increase capillary pressure, it is necessary that the arteries but not the capillaries be dilated, and even then the result is dependent upon certain quantitative conditions.

mind the conditions affecting the permeability of the endothelia themselves. The influence of the capillary tonus, which is under nervous control[1] and regulates the size and possibly also the shape of the capillary stomata must be considered as well. The influence of the latter factor has been pointed out particularly by Meltzer, whose excellent comprehensive presentation of the modern theory of edema[2] will well repay perusal.

ALTERATIONS IN THE CUTANEOUS TURGIDITY

Almost all the appearances which the laity, or we as physicians, designate by the terms "run down," "worn out," etc., depend upon alterations in the turgidity of the skin. The marks of worry, excessive fatigue, fever, collapse, or anything else which mars the beauty of a face depend upon alterations in the turgidity of the skin. The existence of fever is often revealed by an increased turgidity of the skin of the face. Exophthalmic goiter is also characterized by increased turgidity, although emaciation may mask the appearance. In emaciation, pallor, cyanosis, edema, other factors beside turgidity are responsible for the appearances. Diminution in turgidity plus depression of the mimic faculty is responsible for the characteristic facial expressions of the *moribund* and for the so-called *facies Hippocratica* accompanying intestinal obstruction, peritonitis, cholera, etc. In the latter the features seem sunken; the wrinkles and lines of the face more pronounced; the nose sharp; the eyes fallen deep into their sockets; the skin is cool, even cold, and damp with cold sweat; while the color is pale and dusky with cyanosis. In diminished turgidity the wrinkles are very plainly marked on the trunk, especially in cholera morbus or "cholera infantum," where the organism has been deprived of so much water. Oftentimes in cachexia, where the subcutaneous fat is also diminished, the wrinkles become even more marked. A certain grade of diminished turgidity is a physiologic accompaniment of advanced age and senility.

EDEMA

Edema presents a plump swelling and a tense, shiny appearance of the surface of the skin; it obliterates the wrinkles, the hollows, and the normal bony prominences. When the edema suddenly disappears, the epidermis exhibits fine lines and creases and perhaps scales off. When quite fresh, edema often imparts an increased transparency to the skin. Over certain regions, especially the thighs and abdomen, transparent lines or streaks may appear, following the grain of the skin and resembling striæ gravidarum. These lines may remain permanently, even after the disappearance of the edema. They are due to a stretching and distention of the connective tissues and lymph-spaces. Very pronounced edema, especially over areas exposed to considerable mechanical irritation, may be associated with the formation of blebs and blisters in the external layers of the epidermis. If these burst or are opened artificially, a thin fluid will ooze from microscopic openings of the inner surface, sometimes persisting quite indefinitely. As is natural, the danger of infecting these tiny lacerations is considerable, and, of course, serious.

Edematous skin is usually pale because the blood-vessels are compressed by the pressure of the lymph, and the same amount of blood

[1] Nerve-endings have been demonstrated in the capillary walls by S. Mayer.
[2] American Medicine, 1904, vol. viii, Nos. 1, 2, 4, 5.

must be spread over a greater area. Inflammatory edema and edema associated with cyanosis are exceptions to this rule.

Pitting of the skin is quite essential for the diagnosis of edema. It is due to a loss of the cutaneous elasticity, from the distention of the meshes of the tissues by the lymph. Where the skin is very elastic and easily stretched, as on the face or prepuce, the imprint of the finger may vanish almost immediately. Children's skin is so much more elastic than adults' that, even over other parts, pitting may sometimes be wanting. Again, brawny edema which has persisted for some time may pit with difficulty, because there is a certain amount of connective-tissue growth. We notice this particularly in inflammatory edema and in the chronic edema of the lower extremities, which is sometimes converted to elephantiasis.

Edema may be classified etiologically into four varieties:

1. Edema from circulatory stasis, where it may be combined with other transudations, especially into the serous cavities.
2. Edema from disturbances of the renal function, where hydrops may be present elsewhere.
3. Edema from inflammation.
4. Edema from angioneurotic disturbances.

Obstructive or Circulatory Edema.—To explain the origin of general obstructive edema in cardiac patients in accordance with the statements made upon page 49, the following factors must be considered. The slowing of the circulation diminishes the nutrition and the tonus of the capillary walls, making them more permeable, and this effect is most noticeable in those parts most remote from the heart, where, from encountering increased resistance, the circulation is poorest. This increased permeability is also particularly marked in the most dependent portions of the body, from purely hydrostatic reasons, the capillary pressure being directly proportional to the superincumbent column of blood. In these situations we find the first accumulation of fluid in the tissues, because the lymphatics and the venous portions of the capillaries are unable to keep pace with the increased transudation. As an additional factor in a certain degree of obstruction there is also an increase of pressure in the large veins which empty into the heart and receive the lymph from the great lymphatic trunks; this increase of pressure hinders the discharge of lymph into the veins, and thus favors the accumulation of fluid in the tissues. An older explanation of obstructive edema recognized as the only cause the increased venous pressure and the consequent diminished absorption of the lymph in the tissues.[1] The preceding theory, on the contrary, lays the greatest stress upon the augmented permeability of the capillary walls, and takes cognizance of the fact that the general venous pressure is sometimes excessively increased without a trace of edema and that edema may exist with obstructive conditions in which the venous pressure is not increased (vasomotor obstruction, cardiac obstruction with dilated veins). An explanation based solely upon the pressure relations is, therefore, inadequate. The more recent theory is also favored by the fact that it agrees with Meltzer's views in reference to the influence of the capillary tonus upon permeability (see p. 50), and may be used without modification to explain those cases of circulatory disturbance with edema in which there is no demonstrable interference with cardiac dynamics but in which the obstruction is due simply to the vasomotor system.

Any affection of the heart or of the lungs which will produce cyanosis from congestion may also produce obstructive edema. The edema

[1] This view is founded partly upon a confusion of the conditions existing in general venous congestion with those present in local venous congestion produced by the local obstruction of a venous trunk. In the latter the venous pressure above the obstruction is considerable (almost equal to the arterial pressure) because the vein has been transformed, as it were, into a blind manometric appendage of the capillaries and arteries. In general venous obstruction, on the other hand, the venous pressure is in many cases not raised at all or at most the increase of pressure is limited directly to the area up stream from the heart.

begins and becomes most intense in the body parts most remote from the heart and where the capillary walls are most influenced by hydrostatic pressure due to the dependent position of the part, *e. g.*, the hands, the feet, and, in the recumbent posture, the loins (see above). In obstructive conditions the hydrostatic pressure of the blood-column exerts a particularly marked influence; for all these conditions are characterized by a fall of capillary pressure in the general circulation in those positions subjected to the least hydrostatic pressure. The author emphasizes this fact because it is in opposition to some existing hemodynamic theories. Obstructive edema appears late in the face, principally because the arterial and venous blood-columns exert a hydrostatic suction upon the capillaries of this region. Nevertheless there are exceptions to these rules of localization which are not very well understood and probably depend upon vasomotor phenomena. The influence of gravity upon the distribution of the edema becomes very evident with change of posture; *e. g.*, ambulatory patients will

Fig. 14.—Haygarth's nodosities. Case of arthritis deformans (Dr. J. M. Jackson, Massachusetts General Hospital).

suffer from edematous feet; but upon going to bed the edema soon disappears from the extremities and appears in the region of the loins. Lying upon one side for a considerable time will distribute the edema to that side of the body, and, if a hydrothorax be present, will make it more marked upon that side.

When the obstruction is local, the edema will, of course, be confined to the region from which the obstructed vein arises. The edema due to local venous obstruction depends upon an increased pressure in the capillaries (distinguishing it from that due to general obstruction), upon the increased permeability of the capillary walls resulting from the failure of the circulation, and in the more dependent parts upon the lymphatic pressure of the blood-column.

A fluid exudate in the abdominal cavity, due to portal obstruction (cirrhosis, thrombosis) or to a chronic affection of the peritoneum (tuberculosis), will sometimes compress the vena cava inferior or the common iliac veins, and so give rise to an edema of the lower extremities. To decide the true nature of this symptom-complex is often very

difficult, for both ascites and edema of the lower extremities may be coördinated sequences of some general obstruction located in the thorax. The onset will sometimes permit a differentiation. If the abdomen swelled before the legs, the cause will be one of the above-mentioned affections of the abdominal cavity; if the legs swelled before the ab-

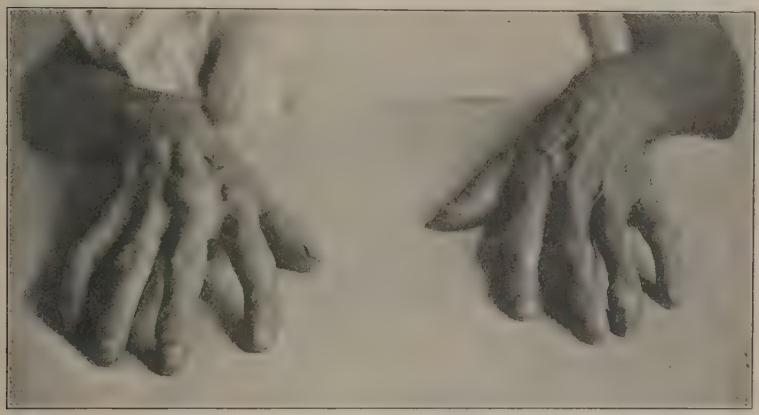


Fig. 15.—Heberden's nodes in arthritis deformans (New York City Hospital).

domen, the cause will be some general circulatory disturbance. The history of the case not infrequently leaves us in doubt.

Renal or Nephritic Edema.—Magnus' experimental researches[1] indicate that hydremic plethora, *i. e.*, an increased volume of the blood due to retention of its water (formerly considered a sufficient cause

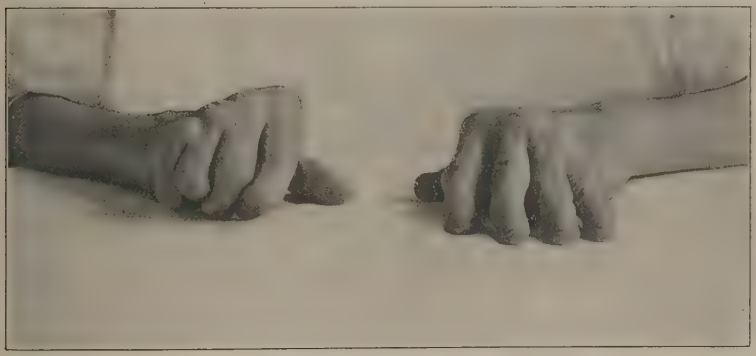


Fig. 16.—Heberden's nodes and ulnar deformity. Case of arthritis deformans (New York City Hospital).

for the production of nephritic edema) may be the cause (although not the only one) of edema and of other transudations if the vessel-walls be coincidentally damaged and rendered abnormally permeable. This latter condition occurs in renal disease from the retention of the urinary solids, and may be produced experimentally by the simultaneous ligation

[1] Arch. f. exp. Path., 1899, vol. xlii.

of both ureters. Only when such a retention exists is it justifiable to assume nephritic edema as the result of hydremic plethora. It should also be noted that the retention of urinary solids requisite to the development of nephritic edema, in addition to injuring the vessel-wall, as indicated by Magnus, may also favor edema by making the tissue-juices hyperosmotic. This is due partly to an accumulation of the metabolic products of the tissues and partly to the transudation of the constituents of the blood which are not eliminated, particularly sodium chlorid. The hyperosmotic fluid attracts the water from the blood.

Nephritic edema, contrasted with the variety due to congestion, is practically independent of the influence of gravity and of the distance of the affected part from the heart. This is due to the fact that the circulation is normal and that the fall of capillary pressure peculiar to general obstruction is not present in nephritis, so that the hydrostatic pressure of the blood-column does not markedly overload the capillary blood-vessels. Its location seems rather to depend upon some peculiar arrangement of the lymphatics in the different parts of the body. Nephritic edema (in acute and subacute nephritis) is a typical example of this selective action, appearing generally in the face, and especially about the eyelids. Edema localized in this way is very suggestive of the diagnosis of nephritis. The more chronic types of nephritis (contracted kidney), however, rarely exhibit any edema until quite late in the disease, and then it usually begins in the feet, because the hypertrophied heart, unable to maintain the circulation against the obstacles in the kidneys and at the periphery, begins to flag. In other words, in these very chronic cases of nephritis dropsy is generally of cardiac origin.

In addition to its early appearance in the face, true nephritic edema is further characterized by the fact that cyanosis is absent, but the possibility of the occurrence of mixed forms must also be borne in mind.

Cachectic Edema.—Under this title are usually included those edemas observed in severe cachexias and particularly those occurring in anemic individuals where there are no pronounced cardiac or renal affections. The latter class is also designated as anemic edema. It is scarcely possible to explain cachectic edema by any one theory, for the factors responsible for obstructive and nephritic edema are evidently active in manifold combinations. It is but natural to suppose that the general disturbance of function in cachectic conditions also affects the heart and the kidneys. We can no longer describe this group of edemas as anemic or hydremic, because neither anemia (or oligochromemia) nor hydremia is present in all these cases; besides experimental investigations indicate that neither oligochromemia nor hydremia is in itself sufficient to produce edema. Even in those cases where we have reason to believe that hydremic plethora as well as hydremia and oligochromemia exist, Magnus' investigations mentioned above show that an additional factor is necessary for the production of edema, namely, increased permeability of the walls of the vessels. Upon the other hand, it is clear that oligochromemia and hydremia, particularly when of long duration, may play an etiologic rôle in these cachectic edemas, since in addition to causing functional disturbances of the circulation and of urinary excretion they may damage the vessels and increase their permeability. According to this conception, cachec-

tic edema will at times simulate the type of nephritic edema, at others that of cardiac or obstructive edema.

Inflammatory Edema.—From the diagnostic point of view inflammatory edema is only important in pointing to some deep-seated inflammation. It must be attributed to the saturation of the neighborhood of an inflammatory focus with the fluid components of the exudate (Samuel).

It is of more interest to the surgeon than to the clinician. Although so rarely present, it is important in suggesting the purulent nature of an underlying pleuritic effusion. In acute articular rheumatism the inflammatory edema about the joints is quite as important as the effusion in the joint itself. Inflammatory edema may aid the surgeon in recognizing a deep suppuration, as in purulent perforative appendicitis, liver abscess, etc. Here it would depend upon adhesions which connect the inflammatory focus with the skin.

Angioneurotic Edema.—Under this heading are included certain rare types of edema of the face or of other areas of the skin. Some of them are combined with analogous conditions in the mucous membranes (laryngeal, bronchial, gastric, or intestinal). On account of their acute origin and rapid *disappearance*, they have been regarded as products of angioneurotic disturbances. The edema of the tongue in Rogowicz's experiments may explain angioneurotic edema. This edema resulted from a maximum dilatation of the lingual vessels and was produced by dividing the vasoconstrictor fibers running with the hypoglossal nerve and simultaneously stimulating the vasodilator fibers which reach the tongue through the lingual nerve. The most probable supposition is that this maximum dilatation of the vessels increases the formation of lymph, raises the capillary pressure, and at the same time renders the capillary walls more permeable. The edema of cyanotic parts should also be included under this heading (see p. 42, et seq.: Œdème bleu des hystériques).

A similar conception possibly applies to some of the edemas occurring in nervous diseases (see Examination of the Nervous System), and to the rapidly appearing circumscribed wheals of urticaria, which are due to local edema and seem to hold a certain etiologic relationship to the previously mentioned idiopathic form. It should, however, be noted that in nervous diseases ending in paralysis (polyneuritis, for example) the loss of motion of the parts has something to do with the occurrence of edema, since it leads to stasis. For the explanation of the origin of urticaria-like edema we must bear in mind the effect of certain organic substances, classified by Heidenhain as the first group of lymphagogues, the action of which is probably due to their influence upon the permeability of the capillary endothelial cells. The type of these substances is furnished by an infusion of crab-meat.

It is difficult to classify the general edema which occurs without nephritis in certain infectious diseases, especially in scarlet fever and diphtheria, as well as that appearing after the injection of diphtheric antitoxin, and that after the employment of potassium iodid.

THE DETERMINATION OF THE ELECTRIC RESISTANCE OF THE SKIN

When the ordinary galvanometers or voltmeters are employed, the determination of the resistance of the body to electric conduction, which resistance is manifested practically by the skin, does not play an important part in electrodiagnosis (see

later). With a galvanometer graduated in milliampères, the cutaneous resistance is naturally included in the measured strength of the current, and if we measure by volts, no attention whatever is paid to the resistance.

The determination of the electric resistance of the skin is, however, of great theoretic and practical interest in exophthalmic goiter and in scleroderma. In the former affection the cutaneous resistance to electric conduction is almost constantly diminished. The explanation ordinarily given, that this phenomenon is due to the increased moisture of the skin, seems doubtful to the author because such a diminution of resistance cannot be obtained in health by flooding the skin with water, and furthermore because the cutaneous resistance to conduction is not diminished in diseases characterized by hyperidrosis, such as phthisis, for example. In doubtful cases this diminution of cutaneous resistance may be of diagnostic value in the recognition of exophthalmic goiter. Upon the other hand, the cutaneous resistance to electric conduction is increased in scleroderma; in these cases there is no doubt that the phenomenon is to be explained by the thickened and dry condition of the integument.

According to Dubois, we must differentiate between the resistance offered by the body to the continuous galvanic current, the resistance to the interrupted galvanic current (immediately after the opening and the closing of the circuit), and the resistance to the faradic current. For the question under discussion we are interested only in the resistance to the continuous galvanic current, since the remaining kinds of resistance have not yet been sufficiently determined and since the above statements in regard to exophthalmic goiter and scleroderma refer to the continuous galvanic current.

From a technical standpoint the cutaneous resistance may be determined by any of the methods employed in physics, but some of these are cumbersome and hence the following is recommended on account of its simplicity. Modern electric outfits are usually provided with some means for measuring the voltage as well as the strength of the current. Now from Ohm's law it follows that an absolute measure of the resistance is obtained in ohms by dividing the voltage by the strength of the current. To determine an increase or decrease of the cutaneous resistance in a given patient we employ the same source of electricity, the same electrodes, and apply them to analogous portions of the body first of the patient and then of the control, a healthy individual. According to Ohm's law, the resistance is inversely proportional to the strength of the current; and the latter is read from the galvanometer in each case. The stronger the current from the same source of electricity in the patient, as compared with that in the control individual, the less the resistance; with twice the current the resistance becomes one-half, with three times the current one-third, and so on. This method is usually sufficient for clinical purposes, particularly when the precaution is taken to employ not only one but several healthy individuals of the same age for comparison. Electrodes of the same size must, of course, be employed and they must be applied to analogous portions of the body, since the resistance to the constant current is inversely proportional to the size of the electrode and since this resistance varies greatly in different cutaneous areas. As the resistance may vary at different times in the same individual, such comparative tests are of diagnostic value only when the difference is considerable. As a matter of fact, the variations from the normal observed in exophthalmic goiter and scleroderma are frequently enormous.

In these determinations, however, still further difficulties are encountered, since the resistance is markedly influenced not only by momentary variations in the voltage, but also by the length of time during which the current is employed. Comparative results can consequently be utilized only when the same voltage and the same length of time are used. Still more accurate results will be obtained by allowing the current to act until the minimum resistance is reached. This minimum, however, varies according to the voltage—the stronger the voltage the smaller the minimum. For every voltage there is consequently a minimum of resistance, which is reached after a certain period of time and which is known as the relative minimum of resistance for the particular voltage employed. This minimum does not decrease indefinitely, but ultimately reaches a point beyond which it remains uninfluenced by further increase in the voltage. This point is designated as the absolute minimum of resistance, and by this we mean the least resistance which it is possible to obtain in any given case by increasing the voltage. In health the absolute minimum of resistance is usually reached with a voltage of 30 to 50, and by an electrode with a surface of 64 to 100 square centimeters.

In exophthalmic goiter Martius, Oppenheimer, Kahler, and others have found that:

1. The absolute minimum of resistance is very low.
2. This absolute minimum is obtained by a low voltage.
3. The relative minimum of resistance for a lower voltage is abnormally low.

The author adds to this that the minima are also usually attained after an abnormally short period of time.

In the Bern clinic the author usually determines the relative minimum of resistance for different voltages up to 10. Two electrodes are employed, each having a surface of 100 square centimeters; they are well moistened and firmly pressed against the abdomen and the lumbar region respectively. Parts with thickened epidermis, as the soles of the feet, are, of course, poorly adapted for these examinations, since the resistance in such situations is markedly influenced by the thickened epidermis and but feebly so by the current.

The following examples are given:

Exophthalmic goiter, electrodes, 100 square centimeters, to the abdomen and back.

Number of Elements.	Volts.	Milliampéres.	Relative Minimum of Resistance (Ohms).	Relative Minimum of Resistance (Ohms) in a Normal Person.
2	2.5	1.0	2,500	10,000
4	5.0	3.4	14,706	6,875
6	7.5	7.6	986	4,444
8	10.0	13.0	769	2,615
10	12.0	20.0	600	15,129

Scleroderma (according to H. Schnyder).

RELATIVE MINIMUM OF RESISTANCE IN OHMS

Volts.	Nuchal-Frontal Region.		Nuchal-Anterior Cervical Region.		Arm-Forearm.		Both Palms.		Both Soles.	
		Normal		Normal		Normal		Normal		Normal
1.38	14,000	(7333)	14,000	(14,000)	28.000	(5600)	28,000	(1500)	5600	(2000)
4.20	11,633	(1663)	14,000	(4,536)	42,000	(3185)	19,090	(1500)	6000	(2000)
8.30	5,375	(521)	8,600	(1,374)	22,631	(1219)	21,500	(1500)	6000	(2000)
14.00	.....		2,978	(609)	11,833	(634)	22,903	(1500)	6714	(2000)

EMPHYSEMA OF THE SKIN

This is due to the presence of gas (generally air) in the meshes of the subcutaneous tissues. Upon mere inspection, emphysema of the skin resembles edema. Palpation, however, over emphysematous regions produces a peculiar crackling, audible as well as palpable. It is due to the movement of bubbles of air in the tissues. Percussion elicits a tympanitic note. (See Percussion.)

In very rare instances the gas is developed in the skin by the activity of gas-producing bacteria, *e. g.*, in *anthrax* and in *malignant edema*. In most cases air penetrates the subcutaneous tissues from the rupture of some air-containing organs or from some external wound. The most frequent source is through the mediastinal connective tissue, resulting from an ulcerative destruction of the esophageal wall (carcinoma) or from a rupture of the pulmonary alveoli (following coughing or external trauma). The emphysema will then first be noted at the lower part of the neck or over the manubrium. In a patient with a tracheotomy wound, air may be forced under the skin by a fit of coughing. The chief diagnostic significance of cutaneous emphysema is its dependence upon the rupture of some air-containing viscus. If the source persist,

the entire body surface may be swollen; but ordinarily the air is readily absorbed and the cutaneous emphysema disappears.

Fig. 17.—Emphysema of left breast and chest-wall, due to broken ribs (Massachusetts General Hospital).

CUTANEOUS HEMORRHAGES

Hemorrhages into the skin appear as spots of variable size, at first red, later violet to black, gradually changing to green and yellow, and finally disappearing. These changes in color are due to the alterations in the blood-pigment. In contrast to hyperemic spots, cutaneous hemorrhages do not disappear under pressure. They are not usually elevated except in certain types of *purpura*, where the epidermis may be raised like a bleb. Absorption of the hemorrhagic spots usually begins in the center. When small, pin-point in size, they are called *ecchymoses* or *petechiæ*.[1]

Cutaneous hemorrhages occur:

1. From *trauma* (ordinary black-and-blue spots). The ecchymoses caused by *flea-bites* (purpura pulicosa) belong to this group and may be mistaken for a form of purpura. They are, however, unlike purpura, found most abundantly upon the trunk. They frequently exhibit the bite-mark as a dark spot in the center of the hemorrhage, and when

[1] [We usually characterize the larger, more or less irregularly shaped spots as ecchymoses, and limit the term petechiæ to those pin-point in size.—Ed.]

fresh, they are surrounded by a hyperemic zone, the color of which will disappear upon pressure.

2. Spontaneously, in *all severe cachexias and infections* which are associated with a hemorrhagic diathesis; particularly as a characteristic symptom in the various types of *purpura*, in *grave anemias*, especially in *pernicious anemia*, *leukemia* and *scurvy*, in *acute yellow atrophy* of the liver, in *phosphorus-poisoning*, in *ulcerative endocarditis*, in *pyemia*, and

Fig. 18.—Purpura (New York City Hospital).

in *nephritis*, and in the *terminal stages* of certain cases of *pulmonary tuberculosis*.

3. In the hemorrhagic forms of the *acute exanthemata: scarlet fever, measles, small-pox*. These are notoriously more serious and critical than the ordinary types, especially "black small-pox," where the hemorrhage occurs in the interior of the pustules; and still more so that rare, very fatal form, "purpura variolosa," where extensive cuta-

neous hemorrhages occur without the formation of any rash. But there are some cases of measles and scarlet fever which are not much more serious than the ordinary cases, although they are shown to be hemorrhagic by the fact that the coloration of the rash does not entirely disappear upon pressure, and that even during the convalescence slight remains of the rash still show as a pigmentation.

Erythema nodosum (contusiforme) not infrequently simulates bruises of the skin, presenting rather extensive cutaneous hemorrhages upon the extensor surface of the extremities.

4. From *marked venous stasis*, especially when accompanied by severe paroxysms of cough, which suddenly increase the congestion, *e. g.*, *pertussis*, where hemorrhages in the mucous membranes, particularly in the conjunctivæ, are not uncommon.

COLLATERAL CIRCULATION IN THE SKIN

A visible distention of veins or arteries in the skin often suggests some deep-seated obstruction to the circulation, *e. g.*:

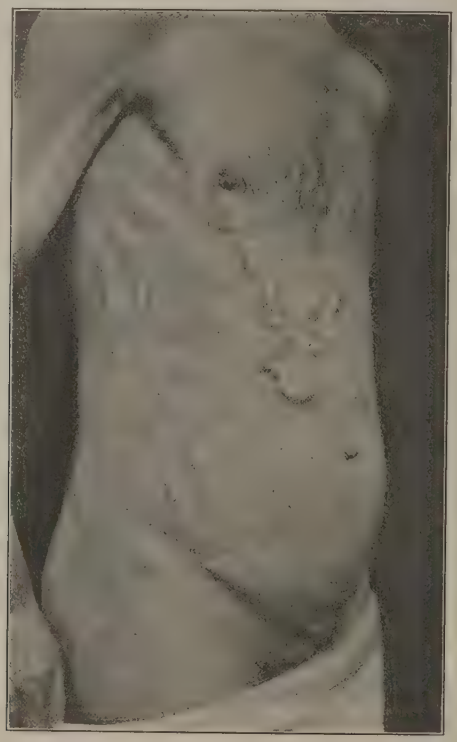


Fig. 19.—Collateral circulation in the abdominal wall (New York City Hospital).

1. The collateral circulation (arterial) when the aorta is occluded at the isthmus. (See Congenital Heart Diseases.)

II. The collateral circulation (venous) upon the anterior thoracic wall. This is of some importance in diagnosing mediastinal or pulmonary tumors, which compress the big veins within the chest, especially the vena cava superior and inferior. Here the intercostal and internal mammary veins dilate and furnish a channel of communication between the two venæ cavæ when either one is occluded.

III. The very striking collateral circulation in the abdominal wall caused by thrombosis of both iliac veins or of the vena cava inferior

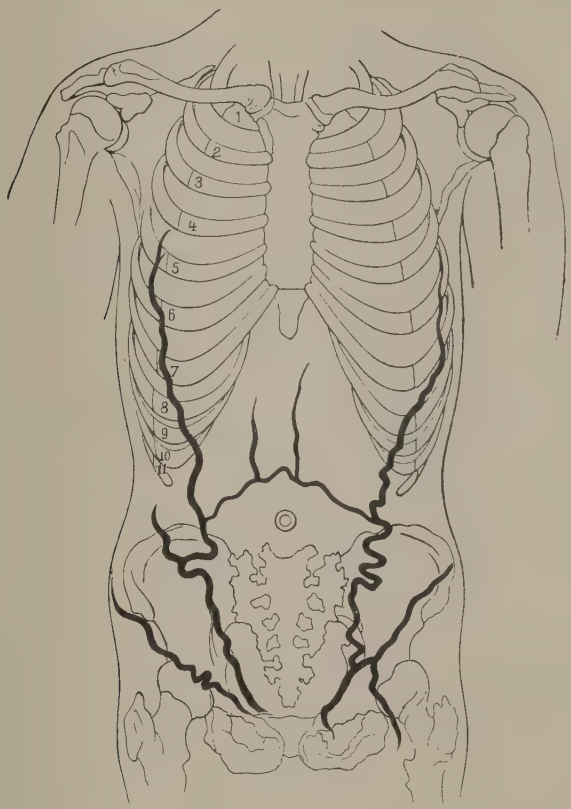


Fig. 20.—Collateral circulation in thrombosis of the vena cava inferior.

(Fig. 20). The blood from the lower extremities, and even from the kidneys, reaches the thorax by way of distended tortuous veins, which are arranged longitudinally and are more pronounced upon the sides than upon the front of the abdomen. This selection of the sides of the abdomen is of some importance in distinguishing this form of obstruction from the next.

IV. The collateral circulation caused by obstruction of the portal veins (cirrhosis of the liver or portal thrombosis, Fig. 21). In the latter

case it is furnished by anastomoses between the tiny veins at the root of the mesentery and those of the peritoneal covering and suspensory ligaments of the liver, even sometimes by a patent vena umbilicalis. In this latter type of anastomosis the distended veins of the abdominal wall are apt to be very characteristically arranged about the navel, forming the so-called "caput medusæ."

Figs. 20 and 21 illustrate the diagnostic distinction between the distention of the abdominal wall veins, due in the one case (Fig. 20) to

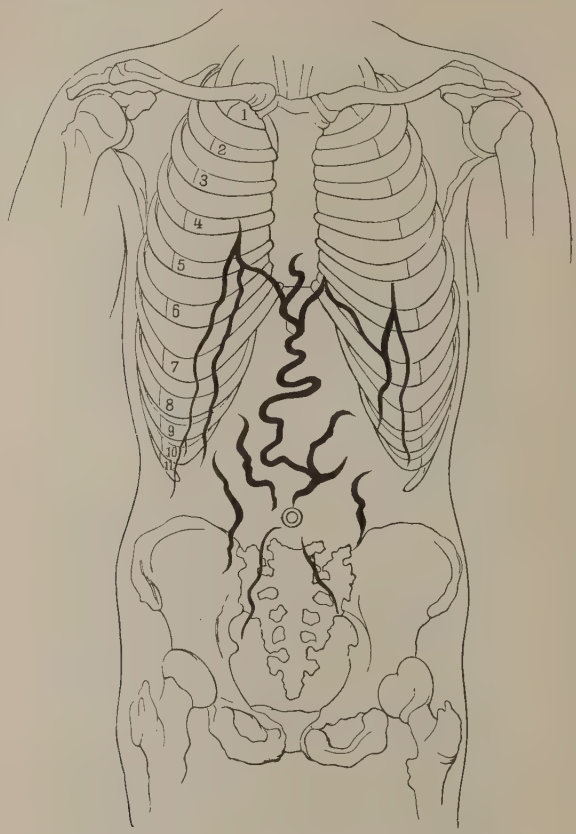


Fig. 21.—Collateral circulation in thrombosis of the portal vein or in hepatic cirrhosis.

obstruction in the vena cava, and in the other case (Fig. 21) to obstruction in the portal system. Numerous exceptions make this distinction less valuable for diagnostic purposes, *e. g.*, when ascites follows portal stasis the presence of the fluid in the peritoneal cavity will naturally produce a secondary obstruction in the vena cava, and collateral veins will form on the sides of the abdomen.

In any of these cases of collateral venous circulation it is always important to determine the direction of flow of the venous blood. This

is readily done, particularly when the valves of the veins are intact, by emptying the blood from the vein by means of pressure with the fingers, and then, when the pressure is removed, by watching, first at one end and then at the other end of the vein, to see from which direction the blood comes first. If there be no valves or if the valves be incompetent, this test is valueless, because the blood would stream back with equal rapidity from either end.

A very fine, irregular, dendritic enlargement of the thoracic skin veins is often observed in all chronic affections of the lungs and pleuræ, especially when adhesions are present between the two pleural surfaces. It probably represents a collateral circulation between the lung and skin. In the very chronic forms of phthisis it is observed frequently, and then quite often in the supraspinous fossa.

Nearly twenty-five years ago the author described a zone of small dilated cutaneous veins which are arranged dendritically and extend in the form of a band about 1 to 3 cm. broad along the anterior lower border of the lung and over the superficial cardiac dulness.[1] It has no especial pathologic significance, because it is also observed in perfectly healthy individuals; but clinically it represents a rough picture of the position of the lung borders. It may be situated either within or without the pulmonary margins, but is generally near by, unless modified in some fashion, as by pleural adhesions. Percussion-results prove that a low position of this zone corresponds to emphysema of the lungs.

It is very difficult to explain the appearance of this zone of vessels, but, without question, it is due to a difference in pressure between the inside and the outside of the chest-wall. Suppose we take the region where the zone of vessels marks the internal pulmonary hepatic boundary. Above the intrathoracic pressure is negative, and below the intra-abdominal pressure is positive, which, of course, in and of itself explains nothing. Respiration, however, alters the pressure relations (see p. 85 et seq.). It produces a distinctive change of shape in the chest-wall, as evidenced by the normal inspiratory sinking in of the lower intercostal spaces and by the so-called diaphragm phenomenon. Both these conditions furnish an inspiratory, localized, girdle-shaped depression of the chest-wall, which must occasion a rhythmic obstruction to the venous blood-current, because the superficial veins of the depressed parts are compressed by the external atmospheric pressure. Now it is conceivable that this rhythmic congestion may give rise to an area of small distended veins. Perhaps a similar explanation would account for the formation of the zone which surrounds the heart, because evidently similar differences in pressure exist at that portion of the chest-wall against which the heart beats and at that portion against which the lung rests. In fact, one oftentimes sees an inspiratory retraction of the intercostal spaces surrounding the cardiac area, quite similar to that about the lower margin of the lung. Local variations in pressure caused by the maximum distention of the heart and its minimum size during systole would also influence the circulation in the thoracic wall. Paroxysms of coughing were formerly considered to be the most important, if not the sole, cause of this vascular distention. They probably do exert a considerable influence, because during a cough the strong positive pressure from the inside causes a marked congestion of the subpleural and subperitoneal veins. This in turn reacts upon certain cutaneous veins which are connected with the subserous veins, and the congestion will be marked along the lines of attachment of the diaphragm. The latter, to a certain extent, acts as a watershed for the venous blood flowing upward and downward. Every one with a cough does not present this zone of veins, so that we must assume as another factor in its origin a certain indefinite abnormal distensibility of the smallest vessels. As a matter of fact, it is found oftenest in such patients as exhibit a similar tendency to the formation of dendritic venous dilatations in other parts of the skin.

[1] Ueber das Vorkommen und die diagnostische Bedeutung einer Zone ektasierter feinster Hautgefässe in der Nähe der unteren Lungengrenze, Correspondenzbl. f. Schweizer Aerzte, 1885.

TROPHIC AFFECTIONS OF THE SKIN

The so-called "decubitus" and the trophic disturbances accompanying nervous affections will be considered later under Examination of the Nervous System.

Clubbed fingers, the peculiar swellings of the terminal phalanges of the fingers, are observed in congenital heart disease, in chronic pulmonary diseases, most frequently in bronchiectasis and empyema (hence the name empyema fingers), and less often in phthisis. The deformity may develop within a few weeks and then disappear again when the causal disease has decidedly improved. In the more chronic cases even the bones share in the deformities. The toes are also affected, though less decidedly. As yet we have little accurate information in regard to the mode of origin.

Fig. 22.—Clubbed fingers (Dr. H. H. Mason).

Fig. 23.—Clubbed fingers (Dr. H. H. Mason).

[Clubbed fingers have also been observed in other cardiac conditions, in suppurative processes elsewhere than in the lungs, in syphilis, in hypertrophic biliary cirrhosis, and in diarrheal affections. The close connection between the exhibition of clubbed fingers and the definitely proliferative changes of some of the bones has awakened considerable interest since Bamberger[1] first discussed 11 cases under the heading "Bone Changes in Pulmonary and Cardiac Conditions," and Marie suggested the name "Osteo-arthropathie Hypertrophiante Pneumonique."[2]

The bone changes *do not involve the distal phalanges*, but more especially the ulna and radius, the tibia and fibula, the metacarpal and metatarsal bones, and very rarely the lower part of the femur. The new bone is usually in layers under the periosteum. The annexed figures (Figs. 22, 23, and 24), especially the skiagram, indicate the appearance very well.

Ebstein[3] begins and closes his thorough résumé with a quotation from S. West, "Clubbing is one of the phenomena with which we are all so familiar that we appear to know more than we really do."—Ed.]

[1] Wien. klin. Woch., 1889, p. 225.

[2] Rev. de Médicine, 1890, vol. x, p. 1.

[3] Erich Ebstein, Deut. Arch. f. klin. Med., vol. lxxxix, p. 67; see also T. C. Janeway, Amer. Jour. Med. Sci., October, 1903, p. 562, and Thompson, Med.-Chir. Trans., 1904, vol. lxxxvii, p. 85.

ACUTE EXANTHEMATA; CUTANEOUS DISEASES; DERMATITIS MEDICAMENTOSA

Although the scope of this book does not include the subject of skin diseases and the acute exanthemata, it seems fitting, from the standpoint of diagnosis, to describe the rash of typhoid fever, herpes febrilis, miliaria, and the medicinal eruptions.

ROSE SPOTS (Roseola)

These are small, round, very slightly elevated, hyperemic, rose-red

Fig. 24, A.—Skiagram of arm and hand with clubbed fingers: *a*, Raised periosteum; *b*, normal bony contour; the space between *a* and *b* shows bony proliferation; *c*, probably a later stage of bony proliferation than between *a* and *b*; *d*, an even more marked bony proliferation of the lower shaft of ulna; the same feature on the inner surface and also on the shafts of the metacarpal bones, especially the second, third, and fourth. A similar, though much less striking, change can be seen on the shafts of the proximal and middle phalanges, but no bony change exists in the terminal phalanges where the clubbing is so pronounced. The styloid processes of both radius and ulna show a osteoporosis (Dr. H. H. Mason, Vanderbilt Clinic, N. Y. City).

Fig. 24, B.—A normal hand for comparison (from L. G. Cole's *x*-ray laboratory).

spots, varying in size from that of a pin-head to that of a small pea. They appear after the beginning of the second week of typhoid fever.

They are sparingly scattered over the abdomen, more rarely over the chest [back.—Ed.] and extremities. Though most marked at the height of the fever, they may persist throughout its entire course and even after convalescence. Relapses are frequently accompanied by a fresh crop of spots. Their hyperemic nature is shown by their immediate disappearance under the pressure of the finger and their instant reappearance when the pressure is removed. Rose spots are differentiated from the rash of acne by the absence of a decided center. This tip in acne is formed by some cutaneous gland or hair-follicle, or by suppuration starting in one of them. The opening of a cutaneous gland or hair-follicle is only rarely found occupying the center of a rose spot, or a vesicle tipping the center. If in doubt concerning any one spot, we can generally find in a case of typhoid fever other absolutely characteristic rose spots elsewhere upon the abdomen. The spots usually pass through a cyclic development, ripening in the course of two or three days and then fading away, while in the mean time new spots appear in other places. In a doubtful case it is often advisable to mark out with a skin pencil the few spots that appear, in order to observe them carefully at each visit. For although rose spots may never appear during the entire course of some few cases of typhoid fever [the positive evidence of this peculiar rash is one of the safest diagnostic signs of the disease.—Ed.]. (See Plate 1.)

HERPES FEBRILIS

This consists of a group of vesicles ½ to 2 cm. in diameter, situated upon a slightly inflamed base. The watery content of each vesicle

Fig. 25.—Herpes cervicalis: Cerebrospinal meningitis (Dr. E. G. Cutler, Massachusetts General Hospital).

rapidly becomes purulent and turbid, and the vesicle then either bursts or dries up, leaving an irregular, scaly crust upon a somewhat reddened background. Although they may appear anywhere upon the face, nose,

PLATE 1.

Typhoid spots (rose spots) in the region of the umbilicus (natural size).

Rose spots in a case of typhoid fever, showing distribution upon the trunk. The three spots upon the face are rather unusual.

cheek, lip, or ear, they develop most frequently on the outer edge of the lip. According to their position they are called herpes labialis, facialis, nasalis, frontalis, and auricularis. The eruption generally appears at the beginning of febrile diseases; rarely in the later stages. It is most common in those fevers with a rapid onset, particularly in croupous pneumonia.

[Howard[1] demonstrated in two cases of labial and nasal herpes and herpes of the body occurring in acute lobar pneumonia pathologic changes in the posterior-root ganglia, the Gasserian ganglia, and the skin. The changes are apparently identical with those shown by Head and Carpenter[2] to be invariably associated with *herpes zoster*. J. R. Hunt[3] has described a similar picture in connection with the geniculate ganglion.

From evidence available at the present date, it is probable that lesions identical in character and similarly localized are present in the herpes of other infectious diseases, and in the light of our present knowledge, that the lesions of the sensory ganglia, nerves, and skin are due to the action of the soluble toxins of various micro-organisms.—Ed.]

Herpes is very rarely observed in typhoid fever, but frequently occurs [in malaria.—Ed.] in epidemic meningococcic meningitis and in pneumococcic meningitis, where it is of value in differentiating these varieties from tuberculous meningitis. There is a certain type of slight ephemeral fever, with nothing objective to be discovered except the increased temperature and herpes, which is termed *febris herpetica*. Herpes, as a rule, is considered a relatively favorable prognostic sign (*i. e.*, as compared with cases of the same disease without herpes). Experience in the use of streptococcus toxin in the treatment of malignant tumors teaches that herpes febrilis depends upon a toxic action; yet in the Bern clinic we have several times isolated meningococci by scraping the base of fresh herpetic vesicles in cases of epidemic meningitis.

The author has noted herpes several times in meat-poisoning; hence its appearance may be of some value in distinguishing this affection from typhoid.

MILIARIA (Prickly Heat); SUDAMINA

Under this head are included various eruptions of tiny vesicles developing most frequently upon the abdomen and chest, and usually accompanied by profuse perspiration. It is generally supposed that this eruption is due to the plugging of the orifices of the sweat-glands with swollen epithelium and to the formation of small retention cysts, some of which may be associated with a slight inflammatory reaction in the neighborhood. Three main types are to be distinguished:

Miliaria crystallina (sudamina; crystal rash): absolutely transparent vesicles, resembling a dewdrop and without reddened base.

Miliaria alba: vesicles with slightly turbid contents upon a faintly reddened base.

Miliaria rubra: small red papules with a faintly developed vesicle in the center. This type is apt to itch.

[1] Howard: Amer. Jour. Med. Sci., February, 1903.

[2] Head and Carpenter: Brain, 1900, Part III.

[3] "On Herpetic Inflammations of the Geniculate Ganglion. A New Syndrome and Its Complications," Jour. Nerv. and Men. Dis., February, 1907.

Miliaria vesicles are generally situated close together. It is as yet unknown whether the eruption in the so-called epidemic miliaria has the character of a specific exanthem or is simply the result of the profuse perspiration.

DERMATITIS MEDICAMENTOSA (DRUG ERUPTION)

Numerous medicinal agents have the peculiarity of exciting in certain individuals eruptions which resemble urticaria, measles, or even scarlet fever. The rash generally fades promptly and disappears when the drug is omitted. Examples of such drugs are most of the antipyretics, especially antipyrin, antifebrin, phenacetin; not infrequently sodium salicylate [and quinin.—Ed.]; many preparations of balsams, *e. g.*, balsam of copaiba; and mercury used externally, or, in rare cases, internally. The injection of antitoxin may produce similar eruptions resembling urticaria, measles, or scarlet fever. Iodid of potassium is apt to produce a rash which may closely resemble erythema multiforme or to bring out a purulent acne-like eruption which may be confounded with syphilis or small-pox. The prolonged administration of considerable doses of bromid of potassium frequently causes an eruption very much like acne. It is usually localized upon the face and chest, and an experienced observer generally distinguishes it by its marked nodular infiltration and bluish appearance. It may develop into suppurating sores covered with crusts which resemble chancroids, and which persist in the resemblance even microscopically by exhibiting a marked overgrowth of epithelium.

OTHER CUTANEOUS MANIFESTATIONS IMPORTANT FROM THE DIAGNOSTIC STANDPOINT

Striæ.—The striæ caused by the stretching of the skin in edema resemble striæ gravidarum, and may persist for some time or even permanently after the edema has disappeared. (See p. 50.) Similar striæ may appear from the rapid accumulation or disappearance of the subcutaneous fat. Any cause which rapidly increases the size of the abdomen, such as pregnancy or the growth of tumors, may produce these striæ.

K. Ziegler's anatomic findings[1] indicate that the striæ arise from laceration of the elastic fibers of the reticular layer of the integument. These fibers undergo but a partial regeneration, so that the original condition is never reproduced.

Desquamation.—In cachexia and emaciation one frequently observes a diffuse, bran-like scaliness covering the skin of the trunk and extremities (pityriasis tabescentium). A characteristic lamellar desquamation of the skin, usually most conspicuous upon the palmar surfaces of the feet and hands, occurs after scarlet fever; a characteristic bran-like desquamation after measles; a more crust-like desquamation after small-pox; and a flaky desquamation after erysipelas.

Furunculosis, as a complication of some general disorder, such as diabetes, is of diagnostic interest to clinicians; otherwise, it concerns only dermatologists.

Scars.—The forms of various scars may be of some importance in considering the past history of a patient, *e. g.*, marks of vaccination, of

[1] Münch. med. Woch., 1905, No. 37.

small-pox, of furunculosis, of carbuncle, of lupus, of inguinal buboes, of tuberculous glands, and the bean-shaped scars of serpiginous syphilids. Unfortunately, even a slight scar does not always persist to show the site

Fig. 26.—Gouty tophi.

of the primary sore of syphilis. Surgical operations, various therapeutic measures, such as moxas, cautery, venesections, leeches, Baunscheidtis-

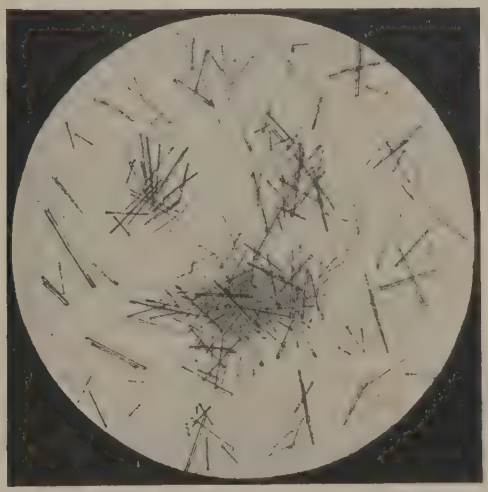


Fig. 27.—Crystals of sodium acid urate from a gouty tophus of the auricle.

mus, and epispastics, and wet-cupping leave behind permanent characteristic scars. They may be important in marking the dates of previous illness.

Gouty Tophi.—The occurrence of gouty tophi in the skin is of diagnostic importance. They are small swellings, somewhat resembling a milium or a small atheroma (wen) varying in size from that of a pinhead to that of a pea. They are most frequently found in the auricle, particularly in the region of the helix, where they are often connected with the cartilage. They usually present a white, transparent center, which upon incision discharges a creamy or chalky mass of sodium acid urate. When placed under the microscope, the crystalline character of the mass is revealed. (See Fig. 27.) It gives the murexid reaction for uric acid. (See Urinary Sediments.)

DETERMINATION OF THE BODY TEMPERATURE

Physicians in ancient times recognized as the principal symptom of fever an increase in the temperature of the blood. But the amount of fever was measured by the acceleration of the pulse. About the middle of the last century Traube, v. Bärensprung, and Wunderlich perfected the methods for taking the body temperature, considering it one of the essential points to be observed in an examination. Since their time the tendency has been to consider that an increase of the body temperature is the essential sign of fever.

The classic symptoms of fever include, in addition, weakness, malaise, anorexia, thirst, digestive and psychic disorders, rapid breathing, alteration in the amount of urinary excretion, and especially "consumption of the body."

Some, though not all, of the above-mentioned symptoms may be produced by an artificial overheating of the body. Certain of them, however, by no means run parallel to the increase of temperature; for sometimes, either with or without antipyretics, the temperature may drop without any especial improvement in the other symptoms. Hence, an increase of body temperature is the most important and constant accompaniment of what we call fever, and to-day the terms are used interchangeably. But still we must not neglect the associated phenomena of the febrile symptom-complex in determining the severity of an attack, because they are partly independent of the temperature, and are sometimes much more important than the amount of temperature increase.

Our conception of fever has been materially clarified by recent writers, and the modern view of this important symptom will be set forth in the following paragraphs.

THE NATURE OF FEVER AND THE PRINCIPLES UNDERLYING ITS ESTIMATION

According to Liebermeister's generally accepted theory, which Hildebrand, Stern, and others have tried to support by recent investigations, fever depends upon an "adjustment" of the temperature regulation to a higher degree in which heat-production and heat-dissipation, the two factors whose product equals the body temperature, are supposed to behave in an entirely different manner depending upon the case, but the end-result is the same, viz., increased body temperature. In the author's (unpublished) lecture upon fever he has proved that this theory is untenable and he has substituted a simpler conception which is more in accord with physiologic and clinical data. This conception will be fully treated in a monograph now in

preparation, but a brief sketch of its salient features may be inserted here. It is unquestionably convenient to regard fever and an increased body temperature as one and the same thing, but from a clinical standpoint this is not entirely satisfactory. Liebermeister's theory is based upon the supposition that there is a special center in the brain for the regulation of the temperature. The author wishes to emphasize particularly that this supposition is unnecessary, to say the least, and that its truth has not been demonstrated. The familiar experiments of Aronsohn and others with heat-stroke prove only that the body temperature may be controlled by the brain through vasomotor influence. This fact alone by no means justifies the supposition of a central regulation of temperature or of the existence of a heat center. Until proved incorrect the author would much prefer to believe that the regulation of the body temperature is a highly complicated process which may be influenced and disturbed by any of the organs, but chiefly by variations in the distribution of the blood. This assumption of a decentralization of heat-regulation explains why so many different conditions result in an increase of body-heat commonly known as fever, and also why factors working in opposition to these conditions may produce a subnormal temperature. The mechanism by which a febrile temperature is brought about seems to the author to be simply as follows: The internal organs are damaged by some toxic substance and there results, according to physiologic laws (acting also in inflammation and functional hyperemia), a vascular dilatation and an increase in the local circulation, in consequence of which the greater portion of the circulating blood is in the internal organs, while the skin, which serves for heat-dissipation, has less than its usual supply. The effect of this changed distribution of the blood is to diminish heat-dissipation, *i. e.*, there is a heat stasis, and, with Traube, the author sees in this the essential character of fever. Increased heat-production is frequently found in acute febrile conditions as an expression of toxic organic destruction, but this is not essential to fever, since there are fevers in which gaseous interchange is not increased. Moreover, the greatest possible increase in heat-production as seen in large eaters and in those doing heavy physical work is unable to raise the body temperature so long as heat-dissipation is sufficient. This idea that fever is due to diminished heat-dissipation seems to be the simplest possible one and one firmly supported by physiologic facts. To assume that fever is maintained by an alteration in the "regulation center," and that external cooling agencies do not easily reduce the fever is to misinterpret the facts in the case. The fact that cooling the surface of a febrile patient has little depressing influence upon the temperature is not due to the action of a regulating center, but rather to a failure in regulation in that the skin is insufficiently supplied with blood, and therefore external cooling cannot be effective. This conception is supported in every particular by clinical conditions. In the first place, it explains the manifold disturbances of function of the organs which accompany fever, only a portion of which can be attributed to the febrile elevation of temperature. Most of these disturbances of function are due to toxic substances and cause the febrile disturbance of the circulation so that the concomitant phenomena themselves will vary considerably in accord with the impaired functions of the viscera. As a consequence of the author's conception of fever as a circulatory disturbance it follows that there must be, to a certain extent, a "fever without fever," a latent fever, *i. e.*, a febrile disturbance of the circulation without an elevation of temperature. This previously inexplicable phenomenon, frequently observed in tuberculous patients (indicated by high pulse frequency, anorexia, etc., *i. e.*, febrile phenomena without elevation of temperature), is at once explained by the supposition that there exists in these cases the typical febrile circulatory disturbance or the increased circulation in the damaged internal viscera, but that, owing to diminished metabolism (anorexia), heat-production is so reduced that the internal temperature does not rise in spite of the diminished heat-dissipation. The occurrence of what the author has designated as "relative fever" is also at once explained by his theory. By relative fever, likewise frequently observed in tuberculous patients, we understand that the temperature does not exceed the usually accepted febrile limit (37.3° C. or 99.1° F. in the evening), but that the temperature is nevertheless higher than we would regard as normal from the constitutional peculiarities of the individual. It is well known that there are individuals whose normal temperature never reaches 37° C. (98.6° F.), and in whom an evening temperature of 37.2° C. (98.9° F.) is consequently to be regarded as febrile and is associated with general febrile phenomena. A further consequence of the author's conception is that fever limits are to be regarded as purely conventional and indefinite. The well-established clinical fact that a wider range in the daily temperature variations may indicate fever agrees very well with his conception and is a special instance of a "relative fever" in which the heat-stasis is shown only by the fact that the increase

in heat-production occurring physiologically during the day (see p. 74) augments the daily temperature variations as a result of the insufficient heat-dissipation.

Furthermore, the author's conception of fever suggests that the fever is purposeful and has a beneficial influence in that the altered circulatory conditions bring more blood to the damaged viscera, but there is absolutely no reason to regard the elevation of temperature in the same light. Such an elevation of the internal temperature due to lessened cutaneous circulation should be considered rather a by-product. This is what we should expect *a priori* from the physiologic adaptation to temperature in the normal subject, even if it had not been proved experimentally that the organism is directly damaged by overheating.

As far as the theory of antipyresis is concerned, the author's conception of fever leads him to believe that antipyresis is a valuable measure provided that the change it brings about in the circulatory conditions is not too violent, too abrupt, nor of too long duration, a conclusion supported by clinical experience. Antipyresis is also recognized as beneficial by the patient himself. From this belief important therapeutic deductions may be made as to the best methods of reducing fever, but their consideration cannot be taken up at this place.

In reference to "sthenic" and "asthenic" fever, see p. 148 et seq.

Before the use of thermometers physicians estimated the temperature by the sense of touch. Though generally this is a perfectly satisfactory method of telling whether or not fever is present, many mistakes may arise. The hand appreciates only the temperature of the skin. This does not always bear a direct relation to the internal temperature of the body or of the blood; because the skin temperature evidently depends not only upon the temperature of the blood, but also upon the amount of blood in the skin at a given time, as well as upon the conditions of heat radiation. For example, during a chill the cutaneous temperature is often diminished as a result of a contraction of the peripheral vessels, while the blood temperature, as shown by the thermometer, is increased. Conversely, the cutaneous temperature of perspiring patients seems increased, provided evaporation and subsequent cooling are prevented by their being wrapped up, because the skin contains an increased amount of blood. Yet the internal temperature need not be raised. These possible sources of error make it plain that thermometers are essential for the accurate determination of the temperature relations. Nevertheless, palpation of the skin is of some value in disclosing the condition of the cutaneous circulation. It is oftentimes accurate, provided that evaporation, chill, and profuse perspiration can be excluded. Perhaps the best place for such palpation, when the patient is in bed, is the back; for there the temperature must be nearly the same as that of the blood. In spite of a high temperature, the skin need not feel very hot to the physician's hand if the room temperature be low and the skin, as well as the blood itself, has been cooled by the surrounding air. This is a point especially to be remembered in considering the possibility of ambulatory typhoid.

THE THERMOMETER

The thermometer carried by practitioners is subdivided in England and America according to the Fahrenheit scale, from 95° to 115°, and on the continent, according to the Celsius scale, from 20° to 45°. To convert Fahrenheit into Celsius and vice versâ:

A° Celsius = $(\frac{9}{5}a + 32)$° Fahrenheit, or

A° Fahrenheit = $(a - 32)\ \frac{5}{9}$° Celsius.

A variety of small clinical thermometers can be obtained in America and in England (perhaps the best are the English make). They are very

accurate, so that an explanation of the method of correcting and tabulating their errors is hardly necessary. [The one-minute Hick's maximum clinical thermometer, furnished with a prismatic lens to magnify the column of mercury, is perfectly satisfactory.—Ed.] The cylindric is ordinarily more convenient than the old-fashioned spheric bulb. The so-called "maximum" thermometers in most common use to-day require vigorous shaking to push the mercury down below the normal point. Then the mercury remains at whatever height it may reach until shaken down again.

METHOD OF TAKING THE TEMPERATURE

The temperature is ordinarily taken by placing the bulb of the thermometer beneath the side of the tongue, and instructing the patient to keep the lips tightly closed during the necessary interval (one to five minutes). Temperatures taken in the mouth are influenced by the temperature of the external air and also by local heat-production on the part of the salivary glands. In some cases it may be necessary to obtain the temperature in the axilla, and, when there is any doubt, in the rectum or vagina. It is hardly necessary to caution a physician to be most careful in disinfecting the thermometer after each time it is used.

In many of the hospitals in Germany a large thermometer is employed. It is left in the axilla from fifteen to twenty minutes. With comatose, stupid, or violently delirious patients or with patients suffering from severe dyspnea or from nasal obstruction sufficient to impede breathing, the temperature must be taken in the rectum or vagina.

[The ordinary one-minute clinical thermometer is sufficiently accurate when used in the mouth, and absolutely so in the rectum.—Ed.]

In any case the temperature should be taken at least twice a day, and under many conditions every two to four hours. When the morning and evening temperatures are taken, the morning commonly represents the temperature between 7 and 9 o'clock, and the evening between 4 and 6 o'clock, which furnishes a practical maximum and minimum without disturbing the patient's sleep. (See pp. 74 and 76.) The temperature is ordinarily indicated upon temperature charts ruled either for every two hours or merely for morning and evening. The normal line is generally printed more deeply or in another color. (See Figs. 34 and 35 for a convenient method of indicating night and day temperatures.)

The temperature-curve alone sometimes suffices to make a diagnosis with considerable certainty; as, for instance, in typhoid fever, pneumonia, chronic tuberculosis, malaria, and suppurative processes. Even a single estimation of the temperature will often throw considerable light upon the diagnosis. Malingering may be excluded if there be decided fever.

THE NORMAL BODY TEMPERATURE

The normal temperature is 0.2° to 0.5° C. (0.4°–1° F.) higher in the rectum or vagina than in the axilla. Von Bärensprung gives the following figures as the normal mean in the axilla at the various ages:

First 10 days	37.75° C. (99.95° F.).
Up to puberty	37.43° C. (99.37° F.).
15 to 20 years	37.19° C. (98.94° F.).
21 to 70 years	36.85° C. (98.93° F.).
80 years	37.26° C. (99.07° F.).

These figures have but a relative value, since they show simply the variations in body temperature for individuals of different ages. They are undoubtedly too high, evidently because of the employment of a defective thermometer.

These, of course, are the daily averages. The daily variation of temperature in a normal person is shown in Fig. 28. The minimum of temperature is observed in the first few hours after midnight; its first maximum is reached during the forenoon, generally between 9 and 10 o'clock; it falls again before the midday meal, rises and reaches a second, the proper maximum, some time between 5 and 8 o'clock in the evening; it then begins to fall until the first minimum is reached. The periodicity of the normal temperature-curve probably depends primarily upon variations in heat-production. The change from waking to sleeping undoubtedly also plays an important rôle, for there have been numerous examples of people accustomed to reversing the day, sleeping in the daytime and working in the night, in whom the temperature variation is reversed.[1]

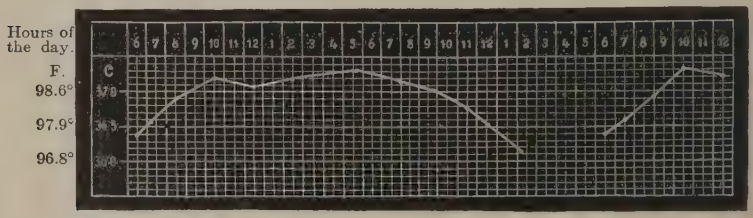


Fig. 28.—Daily curve of the normal body temperature (Liebermeister).

Food and physical exercise influence the temperature. Mountain-climbing, for example, has raised the temperature in normal individuals as high as 40° C. (104° F.). The marked elevations of temperature (as high as 40° C. (104° F.) reported by some observers are undoubted instances of true fever and are to be attributed to pathologic disturbances of internal organs, the muscles being chiefly responsible. The temperature of the external air has some effect upon the body temperature. Sometimes just before a thunder shower a slight rise has been noted in normal individuals. Liebermeister's chart shows that the daily variation amounts to 1° C. (1.8° F.), comparing the absolute maximum and minimum, but to not more than 0.5° C. (0.9° F.), comparing the morning temperature at 8 or 9 o'clock and the evening temperature at 5 o'clock. An evening temperature of 37.3° C. (99.14° F.) is within physiologic limits; although in many individuals, and particularly in consumptives, it would probably correspond to a rectal temperature of 38° C. (100.4° F.), and so indicate fever.

[Unless otherwise stated, these temperatures are mouth temperatures. —Ed.]

[1] Debcynski, ref. in Hermann's Handbuch der Physiologie, 1882, vol. iv, p. 323. Further, U. Mosso: Experienze fatte per invertire le oscillazioni diurne della temperatura nell'uomo sano, Laboratorio di fisiologia nella R. Università di Torino, 7th ed.

FEBRILE TEMPERATURES

Temperatures which exceed 37.3° C. (99.14° F.) are usually regarded as febrile. Wunderlich has computed the following fever scale:

I. Normal temperatures, 37°–37.4° C. (98.6°–99.3° F.).[1]
II. Subfebrile temperatures, 37.4°–38° C. (99.3°–100.4° F.).[2]
III. Febrile temperature:
(*a*) Slight fever, 38°–38.4° C. (100.4°–101.1° F.).
(*b*) Moderate fever, 38.5°–39° C. (101.3°–102.2° F.) in the morning to 39.5° C. (103.1° F.) in the evening.
(*c*) Considerable fever, up to 39.5° C. (103.1° F.) in the morning to 40.5° C. (104.9° F.) in the evening.
(*d*) High fever, above 39.5° C. (103.1° F.) in the morning and above 40.5° C. (104.9° F.) in the evening.

With our present conception of fever (see p. 70 et seq.) these gradations are of but little value. Disregarding the fact that the limit of the normal temperature in this table is at least $\frac{1}{10}$° C. too high,[3] since such sharp demarcations do not exist. According to the author's conception, this table possesses simply a conventional or terminologic value.

Hyperpyrexia.—Very unusual temperatures, 41° or 42° C. (105.8° or 107.6° F.) are spoken of as hyperpyrexia. Teale's case (injury to the spine and recovery) is the highest recorded temperature, 50° C. (122° F.). At the Insel Hospital, Berne, a patient with typhoid fever, who subsequently recovered, once exhibited a temperature of 45° C. (113° F.). Similar cases are quoted in literature as medical curiosities. A temperature above 42° C. (107.6° F.) is rare to-day, because we now have at our command more efficient means of combating fever.

In conjunction with Wunderlich's conventional grades of fever it will be well to recall what has previously been stated at p. 71 in reference to relative fever.

Stern has recently given to the term hyperpyrexia a general pathologic significance, limiting it to those cases in which the heat-regulating apparatus is insufficient, in contradistinction to febrile temperatures where the regulating apparatus is capable of preventing a further increase or an undue diminution. Hyperpyrexia includes, therefore, the excess of temperature added to fever by insufficient heat radiation. Such a differentiation is not compatible with the previously stated conception of fever. (See p. 70.)

PROGNOSTIC SIGNIFICANCE OF HIGH TEMPERATURES

Although a certain significance can be attributed to the height of the temperature, we must be very guarded in making the prognosis of a disease, and must not assume that every high fever is necessarily fatal. In general a typhoid fever with a high temperature-curve is more severe than one with a low range, and in the same patient an increase of temperature generally coincides with some more serious condition or with a complication. The bearing of a certain height of temperature upon the prognosis varies greatly in different diseases. In malarial fever, for example, the temperature may be extremely high without rendering the prognosis more serious; on the other hand, quite innocent throat affections in children are responsible for temperatures of 40° C. (104° F.) or more.

Unverricht[4] has published a collection of abnormally high temperatures in which, nevertheless, recovery followed.

[1] This should be replaced by 37°–37.2° C. (98.6°–98.96° F.), as explained in the following paragraph.

[2] This should be replaced by 37.3°–38° C. (99.14°–100.4° F.), as explained in the following paragraph.

[3] The author believes that the reason why the old boundary given as the uppermost limit of normal temperature was too high, was largely because initial pulmonary tuberculosis was formerly overlooked and the symptoms of such patients were regarded as "neurasthenic," anemic, etc. This false dividing line has exerted a deleterious influence for years, for initial tuberculosis was, and still is, frequently unrecognized sufficiently early.

[4] Unverricht: "Ueber das Fieber," Sammlung klinischer Vorträge, No. 159, p. 724, 1896, Breitkopf and Härtel.

THE FEVER COURSE

DAILY VARIATIONS OF THE FEVER; THE FEBRILE TYPE

The daily course of temperature in any case of fever lasting one or more days is usually much the same as in healthy individuals. If the curve pictured in Fig. 28 were elevated one or two degrees throughout, it would correspond accurately enough to the daily variation of many a fever. But in numerous febrile diseases the maximum or minimum point may appear at a different time; for example, the maximum point may occur in the forenoon or at midday. Again, the daily variations may be much greater than in a normal individual, or in the morning the patient's temperature may be normal or subnormal and in the evening elevated two or more degrees. It is, therefore, evident that to obtain the accurate temperature of a patient with fever we must not be content with measuring the temperature at morning and night alone, but take it at regular, shorter periods, such as once in two hours or once in four hours. An irregular fever is often first discovered by taking the temperature at an unusual time; for example, late at night. A very good indication of the amount of fever is, of course, the patient's feelings; the sensation is not always one of heat, but rather that of general discomfort.

Various types are distinguished according to the variation of the fever during the day. In prolonged or *continued fevers* the daily oscillations rarely vary more than in a normal individual, *i. e.*, not more than 1° C. (1.8° F.). In *remittent fevers* the daily variation is more than 1° C. (1.8° F.). In *intermittent* or *interrupted fevers* the daily minimum is normal or below normal. Since malaria is now so commonly called intermittent fever, it is perhaps advisable to designate this type as *interrupted fever.*

COURSE OF FEVER FOR LONGER PERIODS; COURSE OF FEVER IN A RESTRICTED SENSE OF THE WORD; THE FEVER CURVE IN DIFFERENT DISEASES

The *fever type,* meaning more particularly the daily variations, is of less diagnostic importance than the so-called course of fever or *fever curve,* including a longer period of observation.

EPHEMERAL VARIETIES OF FEVER (SINGLE-DAY FEVERS) [FEBRICULA.—ED.]

Ordinarily these are due either to well-known infections which run an abnormally rapid or abortive course, but whose nature is shown partly by the objective examination, partly by the prevalence of an epidemic of similar cases, or to slight infections of some unknown origin; or to temporary digestive disorders; or finally to some nervous influence, such as hysteria or mental excitement. Children, as is well known, exhibit a transitory rise of temperature from very insignificant causes. In the beginning of an ephemeral fever a diagnosis is almost impossible, so that the height that the temperature reaches will often cause apprehension.

Under this heading is included the fever which appears after *catheterization,* whose origin we do not perfectly understand, and the brief fever following *aseptic operations.* The latter is to be explained by purely psychic influences, such as anxiety as to the result of the operation; by the toxic action of the anesthetic, or of the antiseptics employed; and by the absorption of the relatively harmless secretion of the wound, etc. Where the consistence of the blood is altered by some therapeutic interference, such as transfusion of blood, of salt solution, or of collargol injections, we often observe fevers of similar slight import. In such cases

the origin may depend upon some slight infection or upon fermentative intoxication. In any case these rises of temperature are generally transitory and innocent.

Notwithstanding these numerous types of ephemeral fever no careful physician, in any febrile attack, will neglect a thorough search for some objective explanation or some evidence of infection.

FEVER CURVE OF CROUPOUS PNEUMONIA AND ERYSIPELAS; CRISIS AND LYSIS

There are a number of diseases with continued fever in which the course of the temperature is sufficiently characteristic to furnish the diagnosis. Croupous pneumonia is one of these. It is generally ushered in with a chill, and followed within a few hours by a rapid rise of temperature—39° to 40° C. (102.2°–104° F.)—although shortly before the chill the patient had apparently been feeling well. The fever persists with but slight variation for several days (five to nine days), and then subsides as rapidly as it developed, the drop usually being accompanied by a profuse perspira-

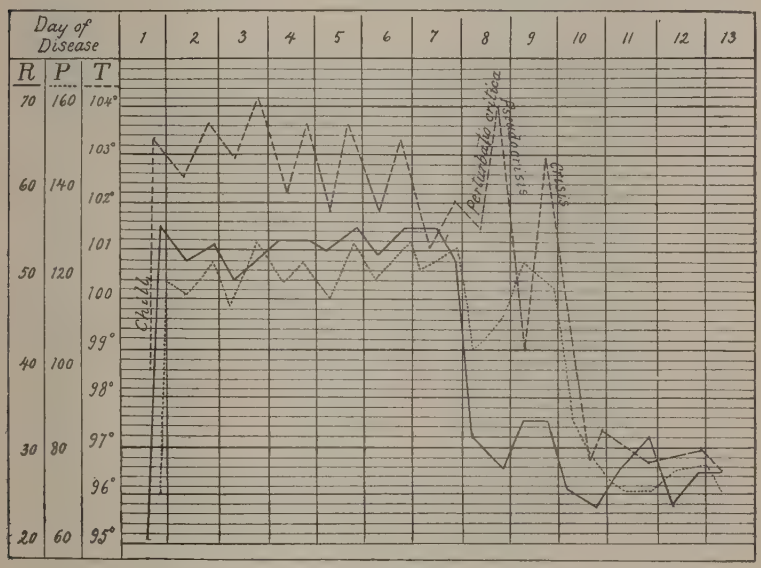


Fig. 29.—Temperature, pulse, and respiration curves in croupous pneumonia.

tion. This sudden drop in the temperature, so characteristic of pneumonia, is called the *crisis*. *Lysis*, in contradistinction, signifies a gradual drop of temperature during two or three days. The latter is rarely observed in croupous pneumonia, but very commonly in many other febrile diseases. A *protracted crisis* is a transitional type between the two. An *interrupted crisis* is a critical drop of temperature interrupted by a transitory rise. A *pseudocrisis* is one in which a critical fall is rapidly followed by a rise and persistence of the fever. A decided rise of temperature associated with a marked disturbance of the patient's general condition, the so-called *pertubatio critica*, sometimes precedes the crisis. All of these conditions may be variously combined in pneumonia (Fig. 29). So far as the fever is concerned, erysipelas resembles it very closely.

THE COURSE OF TYPHOID FEVER

The temperature of typhoid fever is characterized by a gradual, stepladder-like onset, so that each evening it reaches a little higher point than the evening before. The *initial* stage lasts four to seven days; it is followed by a period of continued

high temperature without much of any diurnal variation, the so-called *fastigium* (seven to ten days); and then by a period of remittent fever, the *amphibolic stage*, in which the diurnal variations are very marked, often with a difference of several

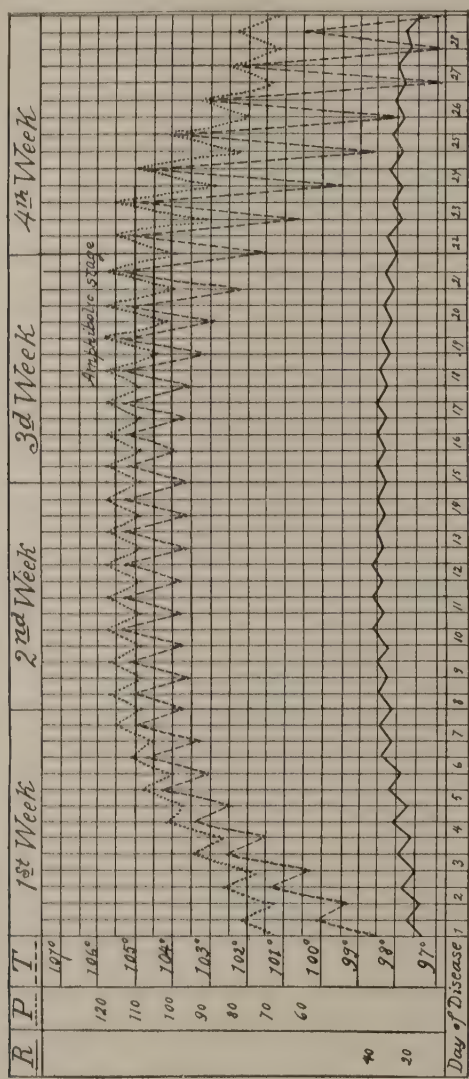


Fig. 30.—Temperature, pulse, and respiration curve in typhoid fever (schematic).

degrees. This lasts five to ten days, and merges into the *defervescing stage*, which is as gradual as the initial rise. The chart (Fig. 30) shows this peculiar temperature curve better than we can describe it.

TEMPERATURE CURVE OF MALARIAL FEVER

The curve of malarial fever (Figs. 34 and 35) is characterized by a critical rise and fall of the temperature every two or three days, associated with the other symptoms of an acute disease. In typical cases the patient feels quite well during

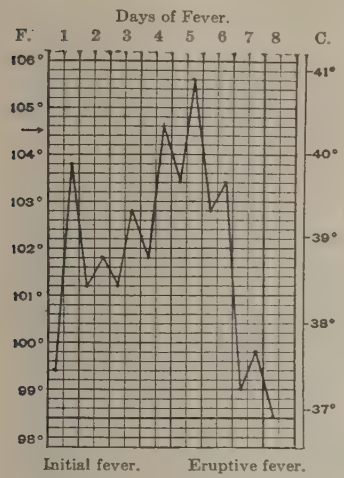


Fig. 31.—Fever curve in measles.

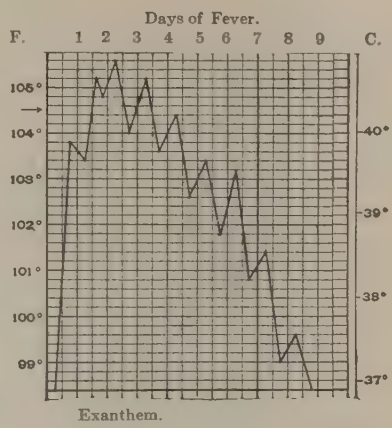


Fig. 32.—Temperature curve in scarlet fever.

the interval; the rise of temperature occurs very suddenly, is accompanied by a marked chill, and is followed later by a sudden drop and a profuse perspiration. The various types are named *quotidian*, *tertian*, and *quartan* fever. As a rule, in

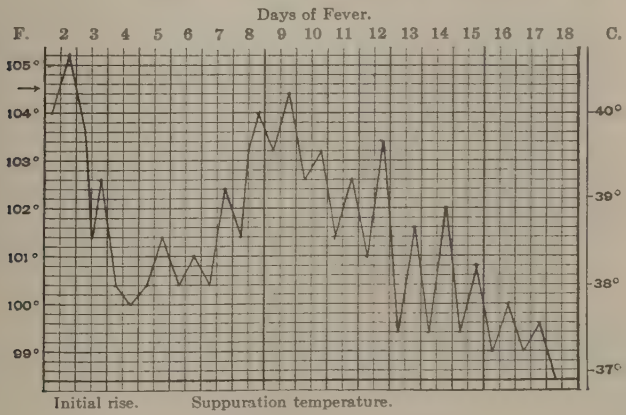


Fig. 33.—Temperature curve in small-pox.

malaria the attacks are repeated at exactly the same hour. Numerous exceptions do, however, occur; in the anticipating variety, the attack of fever appears a little earlier each day; in the postponing variety, a little later each day.

CURVE IN RECURRENT FEVER

As in malaria, so in *relapsing fever*, the temperature curve consists of a number of individual exacerbations. Each exacerbation and each interval, however, persists for several days in recurrent fever (Fig. 36). The relapses may be repeated several times, but finally become shorter and less severe, until complete defervescence takes place.

RELAPSES

In any acute infectious disease there may be a return of the specific symptoms, and especially of the fever, after convalescence has apparently begun, and all symptoms have been absent for some time. Such relapses are most common in typhoid. They should not, of course, be confused with the individual attacks in febris recurrens

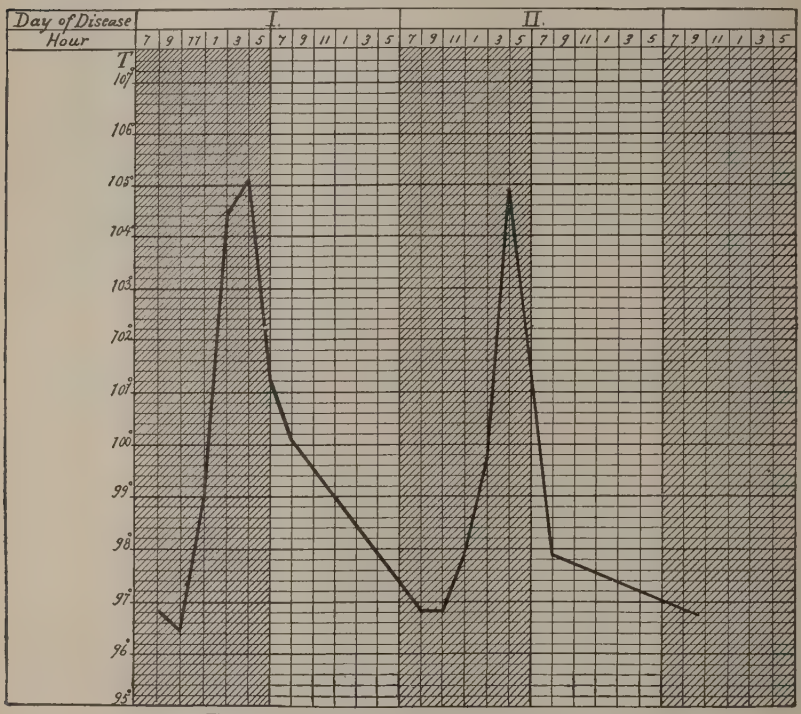


Fig. 34.—Temperature in intermittent quotidian fever.

or malaria, nor with any complication of the original disease; as, *e. g.*, an otitis in measles or scarlet fever. By *recrudescence* is usually meant an intercurrent increase of temperature which resembles a relapse in that it is due to a lighting up of the original disease process and not to a complication, but which differs from a relapse in that it occurs before complete defervescence.

HECTIC FEVER

This is the typical fever of *chronic tuberculosis*. It generally persists a considerable length of time and is of a remittent or interrupted character, with sudden rises and falls. The minimum temperature is usually in the morning and the

maximum in the evening, or the opposite type may occur—inverted hectic fever.[1] A two-hour chart exhibits a very irregular course, with many slight rises and falls throughout the day.

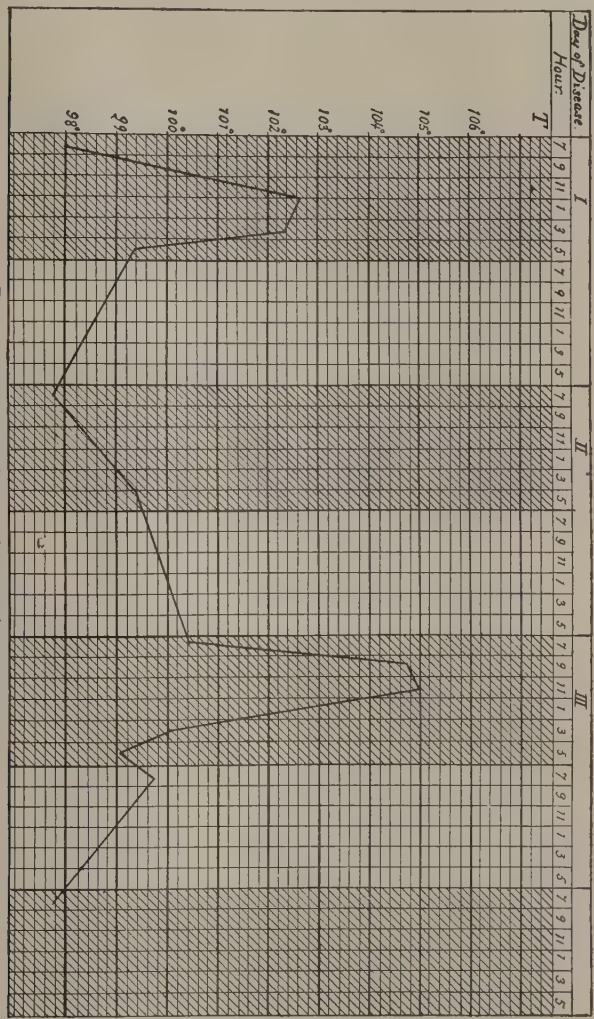


Fig. 35.—Temperature in intermittent tertian anteponens.

Under hectic fever should also be considered that form of relative fever (see p. 71) which manifests itself by an increased range of the daily temperature without reaching the conventional fever limit. It is observed not only in tuberculosis, but also in digestive disturbances.

[1] The cause of this remarkable inversion has not yet been established. Factors which may be considered are: deficient expectoration during the night, increased heat-stasis from too many bed-clothes during the night, increased heat-production during the night from sleeplessness and excitement.

PUS OR SUPPURATIVE FEVER; IRREGULAR CHILLS IN PYEMIA, ULCERATIVE ENDOCARDITIS, AND GALL-STONES; CHILLS IN INFARCTIONS

Though often resembling the chart of hectic fever, that of suppuration is generally more irregular in the time and the degree of the exacerbations and remissions.

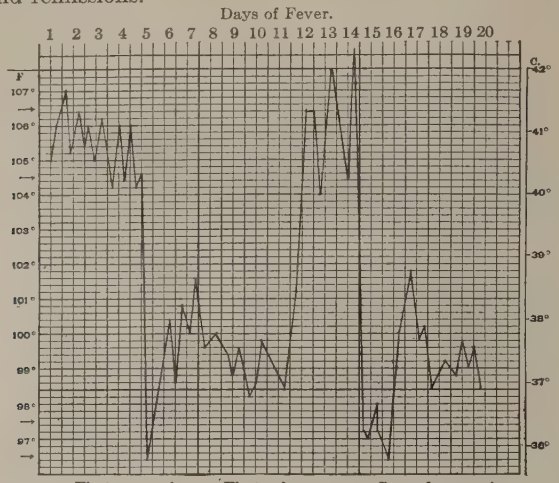


Fig. 36.—Temperature of recurrent fever (Wunderlich).

In pyemia the fever frequently occurs in very intense paroxysms, accompanied by severe chills resembling those of malaria, except that

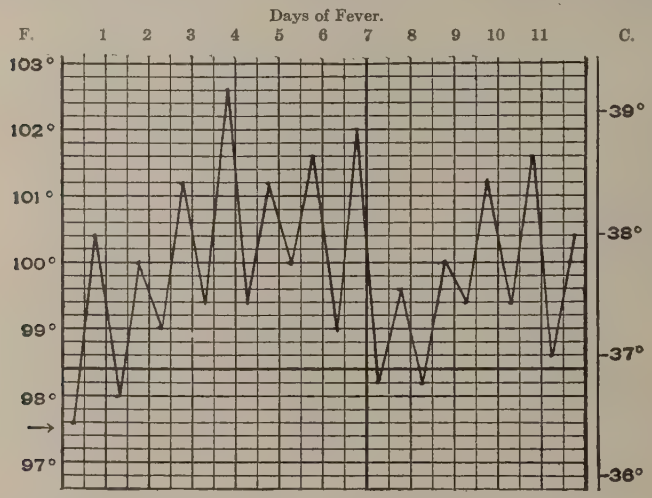


Fig. 37.—Hectic fever in phthisis.

they are more irregular. Closely related to these so-called erratic chills of pyemia are the chills which appear in ulcerative endocarditis and in

gall-stone affections. Non-purulent infarctions are associated with a similar, though less pronounced, chill.

ATYPICAL FEVER

In some diseases there is no type to the temperature course, so that, although the clinical picture is sufficiently constant, the temperature chart alone would furnish very little information of the nature of the disease. Examples are *diphtheria* and *septic processes.*

SUBNORMAL TEMPERATURES

These are quite as important clinically as febrile temperatures.

Wunderlich considers anything below 36.25° C. (95.25° F.) a subnormal temperature.

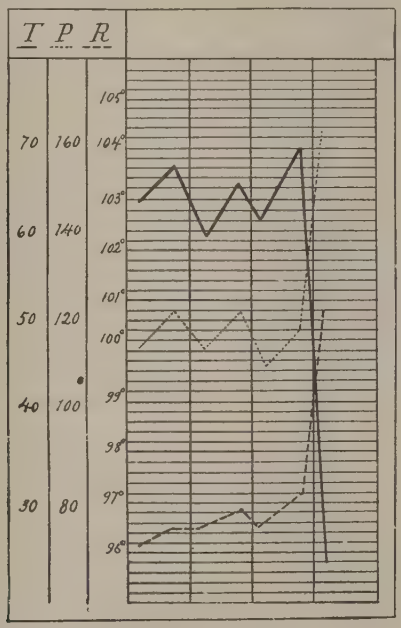


Fig. 38.—Pulse, temperature, and respiration in collapse.

Marked depressions of temperature are noted:

1. In the prolonged action of intense cold.[1] A temperature of 27° C. (80.6° F.), as in a case of freezing, is not necessarily fatal.

2. Following a pronounced critical fall of temperature in fever. After the crisis in pneumonia the temperature often drops to 34° or 35° C. (93.2° or 95° F.).

3. In so-called "collapse," where there is a sudden fall in the temperature. This occurs in very sick patients (especially those with fever),

[1] Compare Glaser, "Ueber Vorkommen und Ursachen abnormaler niedriger Körpertemperaturen," Inaug. Diss., Bern, 1878; and Janssen-Quincke, "Ueber subnormale Körpertemperaturen," Deut. Arch. f. klin. Med., vol. liii, p. 247.

and is associated with marked weakness, numbness, rapid pulse, profuse perspiration, etc. The crisis in pneumonia is sometimes mistaken for a collapse. The pulse, however, in the latter is weak and rapid; whereas in the former it remains of good strength, and diminishes in frequency in proportion to the fall in the temperature. Collapse, though sometimes recovered from, is frequently an immediate precursor of death. The accompanying symptoms are usually attributed to cardiac weakness. Vasomotor inhibition may also be a factor.

4. Sometimes *after a severe hemorrhage;* in *chronic heart and lung diseases,* which lead to imperfect aëration of the blood (cyanosis), and therefore to insufficient oxidation in the various processes throughout the body; further, in *chronic wasting diseases* (carcinoma of the esophagus), where metabolism is reduced to a minimum; in *sclerema neonatorum;* and finally in *mental afflictions,* especially of the melancholic type.

Prolonged subnormal temperatures accompanying such conditions as are mentioned above always indicate a grave diminution of the metabolism or some equally serious disturbance of the heat regulation.

CHARACTER OF THE RESPIRATION

FREQUENCY OF RESPIRATION UNDER PHYSIOLOGIC CONDITIONS

Hutchinson considers the normal respiratory frequency in adults between 16 and 24, or about 1 to every 4 pulse-beats. Quetelet gives for the new-born an average of 44, for the five-year-old child 26, respirations to the minute.

It is a good plan to count the respirations while apparently feeling the pulse, because the patient's attention might otherwise modify the rate. For greater accuracy, the number of respirations should be counted during an entire minute.

Physical exertion will increase the rate of respiration; rest or sleep will diminish it somewhat. A stomach distended by food and drink increases the rapidity of the respiration because the diaphragm excursion is thereby somewhat limited, and also because the oxidation processes of the organism are considerably increased immediately after an abundant ingestion of food. Irritation of the skin may increase or diminish the rate of respiration. Psychic or sensory impressions, movements, clearing the throat, eating, drinking, or smoking will alter the rapidity of the respiration. Before considering that a certain rate of respiration is pathologic we must therefore bear in mind all these physiologic variations.

NORMAL TYPES OF BREATHING

The distention of the lungs with air takes place partly by means of raising the ribs and sternum and rotating the former outward and upward, and partly by depressing the diaphragm. Although in every-

body both these factors take part in the movement of inspiration, yet one or the other is apt to be more prominent, thus producing a more *costal* or a more *diaphragmatic* (*i. e.*, abdominal) type of breathing. Women commonly breathe costally; men, costo-abdominally. This difference, which seems to depend upon the formation of the chest, is naturally very suitable during pregnancy, when the diaphragmatic excursions are interfered with. A child's breathing is essentially costal.

PATHOLOGIC VARIATIONS IN THE TYPE OF RESPIRATION

Either the costal or the diaphragmatic element may be implicated and so alter the type of respiration.

Limitation of Diaphragmatic Breathing.—The excursions of the diaphragm may be impeded by some mechanical interference with its descent, *e. g.*, by a paralysis of its muscular structure; by an abnormal flattening of its vault (in certain types of emphysema); by painful breathing; by an increase in the abdominal contents, *i. e.*, pregnancy, meteorism, abdominal tumors, ascites. *Inflammation* in the vicinity of the diaphragm, *e. g.*, pleurisy, pericarditis, peritonitis, will limit the excursions of the diaphragm, partly on account of the pain and partly from a slight paralysis of its muscle-fibers (especially in diffuse peritonitis, on account of the disturbances in the circulation following the inflammation). Actual diaphragmatic paralysis occurs in *multiple neuritis*, in *progressive muscular atrophy*, etc. In any of the above instances the costal breathing may appear to be increased at the expense of the abdominal effort.

Limitation of Costal Breathing.—Costal respiration may be interfered with in a mechanical way by extensive ossification of the costal cartilages (ankylosis of the articulations of the ribs in arthritis deformans, etc.). Under such conditions the costal type in women and children and the costo-abdominal type in men may become purely abdominal.

DIAPHRAGM PHENOMENON AND ALLIED APPEARANCES (LITTEN'S SIGN)

Although it had been previously mentioned by Stokes and Gerhardt, Litten[1] deserves the credit for calling attention to this almost forgotten sign. He analyzed a series of cases, determined its practical significance, and named it the "diaphragm phenomenon" (Pl. 2). It consists of a horizontally placed shadow observed with inspiration near the lower pulmonary border, most constantly anterolaterally, but occasionally running in a ring around the whole chest. This shadow seems to slip downward, corresponding to the inspiratory descent of the pulmonary margin, as shown by percussion. It is very fittingly named, because, as a matter of fact, it is the most distinctly visible evidence of the depression of the diaphragm. Normally, the moving shadow begins above in the sixth intercostal space, descends with superficial inspiration one to one and one-half intercostal spaces, and with deep inspiration two to three spaces. It intersects the ribs at an acute angle. To show it most distinctly, the patient should lie as flat as possible (without extra support for his head) and with his feet toward the window, so that the region between the sixth rib and the costal margin is lighted obliquely. The observer should stand between the patient's feet and the window, with his eye at a distance of 3 or 4 feet from the lower thorax, the line of vision forming an angle of 45 degrees with the latter. Provided the patient breathes deeply and the light, although not necessarily strong, slants

[1] Deut. med. Woch., 1892, No. 13. "Das Zwerchfellphänomen und seine Bedeutung für die Praxis," Deutsche Aerztezeitung, 1895, No. 1. Verhandl. des Cong. f. inn. Med., 1895.

sufficiently, the phenomenon is generally plain. Even a candle light may be sufficient, but a very diffuse light is unfavorable. There is no corresponding expiratory sign. The flattening of the lower intercostal spaces from below upward during expiration is of quite different significance.

The explanation of Litten's sign is comparatively simple. As the diaphragm in its descent begins to peel off from the thorax and both widens and deepens the complementary pleural sinus, it exerts a suction upon the intercostal spaces just below the margin of the lung. This produces the shadow. It is evident that no analogous process will occur during expiration, because the elevation of the diaphragm is regulated only by the elastic retraction of the lung. In health, particularly in lean individuals, the diaphragm phenomenon is a nearly constant appearance. Marked development of fat or muscle or edema of the thoracic wall will prevent its appreciation, and even under perfectly physiologic conditions it may be sought for in vain. Its presence proves that at the particular place where it is observed, the diaphragm and the lung lie against the thoracic wall, both freely movable; its absence points to the opposite conclusion. Therefore it cannot be made out opposite pneumonic infiltrations nor in those places in pleurisy where the exudation is situated or where the lung is adherent to the chest, nor in hydrothorax or pneumothorax, etc. Litten has called attention to the fact that this sign is of great value in differentiating an empyema from a subphrenic abscess; it is absent in the former, but present in the latter.[1] Under some conditions the diaphragm phenomenon may facilitate a distinction between pneumothorax and diaphragmatic hernia. A broken or irregular shadow is said to point to partial adhesions of the diaphragm to the thoracic wall. The extent of the diaphragm phenomenon will furnish some idea as to the excursion of the lung in emphysema and phthisis. Paralysis of parts supplied by the phrenic nerve is associated with an absence of the diaphragm phenomenon. Since this sign is by no means absolutely constant in healthy individuals, it is evident that its absence upon one side alone is much more important than upon both sides.

We must be careful not to confuse the diaphragm phenomenon with two other conditions which exhibit shadows in the same area, viz., the visible depression of the lower ribs with expiration and the retraction of the lower intercostal spaces with inspiration.

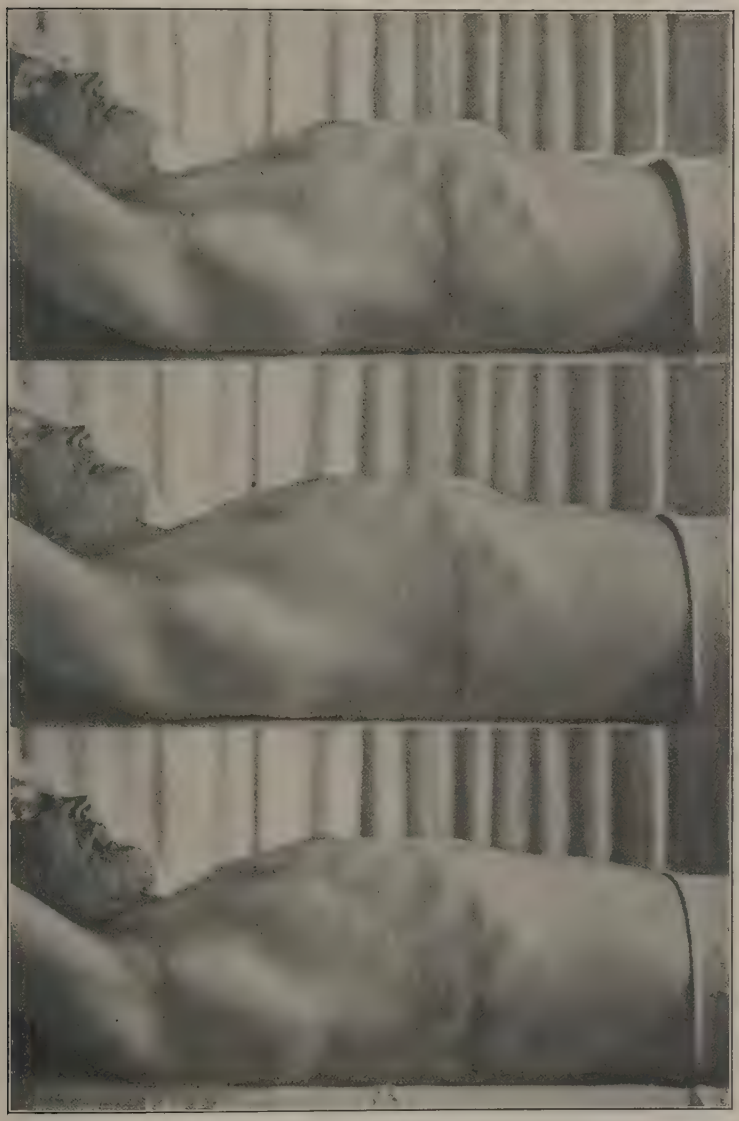
The former, being expiratory, is easily differentiated from the diaphragm phenomenon; but the latter, being inspiratory, is more difficult to distinguish. The lower intercostal spaces situated along the attachment of the diaphragm are under a positive intra-abdominal pressure when the latter is in a position of expiration, whereas they are exposed to a negative intrathoracic pressure when the diaphragm is depressed by inspiration, and therefore they are retraced in the same way as the diaphragm. The physiologic retraction of the lower intercostal spaces as a whole will thus present a descending shadow easily to be confounded with the Litten sign, but a careful observation will detect the difference. The shadow of the Litten sign is linear, passing through the intercostal spaces as a line, while the shadow of the physiologic retraction of the intercostal spaces is more diffuse, each space, one after another, becoming shaded *in toto*. Very often also the descending character of the inspiratory retraction cannot be recognized at all, because the diaphragm in its contraction exerts a suction upon those intercostal spaces from which it has not yet separated. A further distinction is that an exactly opposite movement from below upward takes place during expiration, *i. e.*, an expiratory bulging. This does not occur in the diaphragm phenomenon.

The depression in stenosis of the air-passages, and the essentially identical peripneumonic retraction, differ from this physiologic retraction in that the appearances are very much more marked in the former, affect the ribs as well, and are not confined to the intercostal spaces in the territory of the diaphragm.

In cases where the diaphragm phenomenon was not plainly recognized, the author has succeeded in bringing it out very plainly by faradic stimulation of the phrenic nerve. With sufficient current the diaphragm contraction follows so quickly and energetically that the phenomenon is often much plainer than with ordinary breathing. In this way we may bring out very plainly differences between the two sides.

[1] It is well, however, not to lay too much stress upon this statement, because, although its existence in the latter condition has been demonstrated, we can as yet scarcely be sure that the diaphragmatic movement is not sometimes impeded by a subphrenic abscess.

PLATE 2.



Diaphragm phenomenon (Litten's sign), from a patient with fibroid phthisis of left lung (New York City Hospital). The linear shadow has been emphasized in the reproduction of the photographs.

1. *Full Expiration.*—Note the height of the shadow and the slight concavity of the abdomen corresponding to the respiratory phase.

2. *Medium Inspiration.*—Note the descent of the linear shadow and the slight change of contour of abdomen corresponding to the respiratory phase.

3. *Deep Inspiration.*—Note the further descent of the linear shadow and the rigid abdomen corresponding to the respiratory phase.

Although the artist has intensified the shadow in the reproduction, the excursion of the right lung and right side of the diaphragm were so pronounced in this patient that the distance between the shadows in the extreme positions of respiration was greater than has been represented. The patient's left lung was practically useless; hence the abnormal extent of the right lung's excursion.

ASYMMETRIC RESPIRATION AND PATHOLOGIC INSPIRATORY RETRACTION OF THE CHEST

An obstruction to respiration which affects but one lung will cause asymmetric breathing; the diseased side will make a less extensive excursion and will also lag somewhat behind the healthy side. The conditions which may give rise to such a unilateral limitation of breathing are: the various types of pulmonary consolidation (pneumonia, phthisis, tumors); pleurisy with effusion or pleurisy merely with the formation of fibrous bands and tough adhesions; and pericarditis with effusion. Asymmetric respiratory excursions may be appreciated by inspection, but they will oftentimes be much better appreciated by palpation. With one hand placed upon each side, the examiner can at the same time appreciate an asymmetry of the chest contour. The chest, half of whose mobility is diminished, may be either expanded or contracted, as explained upon p. 34 et seq.

Compare p. 93 et seq. for the occurrence of inspiratory retraction in the jugulum (suprasternal fossa), epigastrium, and flanks with stenosis of the upper air-passages.

But without any stenosis similar local retractions occur over parts of the lung area where the normal inspiratory distention of the lung is prevented by atelectasis or by consolidation. This retraction, especially when it occurs quickly and violently (as with dyspnea), is due to the variation in the inspiratory negative pressure within the interior of the chest, which draws in the more expansile portions of the lung along with the overlying portions of the chest-wall under the influence of the external atmospheric pressure. We see this particularly well marked in the catarrhal pneumonia of children, whose soft and more flexible chests favor the retraction. It is called a "*peripneumonic retraction*" or a "*peripneumonic groove.*" It is generally situated in the lateral and anterior region of the chest along the lower lung border, even when the pneumonia is, as usual, situated in the back. This probably depends upon the fact that the inflexible consolidation located in the back interferes mechanically to a certain extent with the excursions of the lung margins at the sides and in the front, and that the anterior and lateral portions of the chest are especially flexible. Peripneumonic retractions are, however, sometimes observed posteriorly, near the inferior pulmonary margin. The direct pull of the diaphragm, just as in stenosis of the upper air-passages, may, in addition to these mechanical factors, help to create a peripneumonic depression. (See p. 94.) The epigastrium and the jugulum, too, may be retracted in a similar way in pneumonia, so that in small children the diagnosis of croup is not infrequently suggested. The inspiratory stridor and hoarseness of the voice and of the cough in the latter ordinarily facilitate a distinction. Peripneumonic retraction must not be confounded with the normal inspiratory depression of the lower intercostal spaces, the explanation and differentiation of which have been discussed upon p. 86 et seq. In pneumothorax also the author has seen marked retraction of the lower portion of the thorax, doubtless due to direct traction by the diaphragm.

D. Gerhardt[1] has called attention to another cause of inspiratory retraction of the lower thoracic margin. Besides the diaphragm's well-known effect upon the

[1] Zeit. f. klin. Med., 1896, vol. xxx, Nos. 1 and 2.

inferior surface of the lung, Duchenne demonstrated that, by resting on the abdominal contents and moving over the parts contained in its vault, as over a roller, it has in inspiration the action of lifting the margin of the thorax. If this decided elevation of the lower ribs be prevented by immobility of the costal articulations or by the horizontal position of the ribs, as in some emphysematous chests, or by the lack of any firm point of attachment of the abdominal contents in enteroptosis, then during inspiration the contraction of the diaphragm will depress the chest-wall inward.

ABNORMALITIES IN FREQUENCY AND RHYTHM OF THE RESPIRATION (not Including Dyspnea)

Alterations in the frequency of respiration depend, for the most part, upon difficulties of pulmonary aëration or upon increased demands upon the lung, and will therefore be considered and explained with the symptom-complex of dyspnea in the following chapter. Only in very rare instances are changes in the frequency of breathing independent of dyspnea.

To this group belongs the diminution of respiratory frequency (oligopnea) found in certain unconscious states, especially in severe brain affections (meningitis, hemorrhage, or in tumors of the brain); uremia; diebetic coma; severe infections; some cases of poisoning, and in a similar way in the final agony. Irregularity of the respiration may be noted as well in any one of these conditions. Unquestionably these disturbances are distinctly dependent upon an alteration in the function of the respiratory center.

Either one of two very characteristic types of pathologic breathing, each one associated with a change in the rhythm, and arising under exactly similar conditions, may occur instead of the slowed respiration just mentioned. These are the so-called Biot's or meningeal and the Cheyne-Stokes respiration.

Biot's respiration, especially common in meningitis, may also occur in other cerebral disorders and in other grave general conditions. It is characterized by very decided pauses in the breathing, which last from several seconds to half a minute or longer. They are more or less periodic, but at times are irregularly repeated. It is a phenomenon of grave prognostic significance.

Cheyne-Stokes respiration is characterized by similar long pauses in the breathing. It differs, however, from the above by the fact that the breathing begins very slowly and superficially after the pause, gradually increases in depth and intensity to a maximum, diminishes again, and finally stops entirely, thus producing another respiratory pause. It is, therefore, a distinctly periodic type of respiration. It occurs under similar conditions to the Biot's meningeal respiration, especially in grave affections of the brain, of the respiratory and of the circulatory organs, and quite frequently in arteriosclerosis and chronic nephritis. Although more frequently observed in the unconscious, it is not uncommon even when consciousness is maintained, especially in patients with chronic respiratory or circulatory disorders. In these affections consciousness oftentimes oscillates with the respiration, is periodically obliterated during the pause, and returns again when respiration is resumed. There are other phenomena more or less characteristic. During the pause in the breathing the rate of the pulse may be decidedly slowed, its tension may be altered, and the pupils may be contracted.

Very often, though by no means always, patients have a subjective sense of dyspnea during the period of increasing respiration; and if unconscious during the pause, they are awakened, as they express it, by a sensation of suffocation or dyspnea. Cyanosis usually accompanies the onset of the dyspnea, and it may sometimes even increase with the augmentation of the breathing. With some patients Cheyne-Stokes respiration occurs only during sleep. Medicinal doses of morphin usually intensify the phenomenon and may even originate the condition. Generally speaking, the prognostic significance is very grave, although not invariably fatal. According to the severity of the causal condition, the symptom is either transitory, or else one directly preceding death. Only in cardiac or renal disease has it ever been observed to persist for some months.

The explanation of Cheyne-Stokes respiration is still not wholly agreed upon. It is indisputable that, like meningeal breathing, it depends upon a diminished excitability of the respiratory center. This seems to be the only part of the explanation beyond a doubt. Traube's original theory assumed that the symptom arises when the excitability of the respiratory center is so decidedly diminished by the insufficient supply of oxidized blood resulting from the circulatory disturbance that, at a certain moment coinciding with the first breathing pause, there is no longer a sufficient physiologic stimulus to arouse the respiratory movements. With the cessation of respiration the blood becomes still more decidedly venous. This irritates the respiratory center intensely, so that, despite its diminished susceptibility, breathing begins again. This in turn diminishes the venous character of the blood, and the breathing gradually becomes weaker in proportion to the oxidation of the blood.

Traube's explanation does not make it very clear why the breathing increases gradually nor why the second respiration is stronger and deeper than the first. For as soon as breathing begins, the venous character of the blood must immediately lessen the respiratory center's irritation, and so the second respiration should be weaker. Traube explains that the first breath is so diminutive that it cannot affect the venous character of the blood, and so cannot lessen the irritation to the respiratory center; but that, on the contrary, the irritation increases despite the return of breathing, until it—the irritation—reaches a maximum. Such a hypothesis will explain the peculiarity that the patient appears most cyanotic and complains most of the subjective sensation of dyspnea during the period of increasing respiration. Another objection to Traube's explanation is that, after an improved supply of oxygenated blood has once restored the respiratory center's normal excitability, there is no apparent reason for the breathing fading away again. If we believe, with Traube, that asphyxia of the respiratory center is the sole cause of its diminished excitability, the objection cannot be answered. If, however, we regard the diminished excitability as entirely or partially independent of the asphyxia and more self-dependent, the objection loses its force. Evidently, then, if the blood be better aërated, the intense irritant to the respiratory center will be removed, although the latter's sensibility has not been improved. Hence, the breathing will gradually diminish in frequency in proportion to the improvement in the oxidation of the blood.

With these modifications, Traube's theory seems plausible enough. Partly on account of the difficulties mentioned above, numerous other

explanations of Cheyne-Stokes respiration have been advanced. We will mention only two of these which are the most generally known, viz., Filehne's and Rosenbach's.

Filehne's hypothesis, beginning with the pause in respiration, assumes that the venous condition of the blood irritates the vasomotor centers and so produces a spasm of the cerebral vessels. Therefore the respiratory center, whose irritability has already been reduced, becomes anemic. This anemia acts as a further irritant to respiration. As soon as the breathing has again oxygenated the blood sufficiently, the vascular spasm vanishes, but the respiratory stimulus is not sufficient to continue the breathing, hence the pause reappears. Filehne's theory is more complicated than Traube's; the same objections apply to it; and more accurate investigations seem to have disproved completely any such relationship between the vasomotor center and Cheyne-Stokes breathing.

Rosenbach maintains that the periodicity of this type of breathing results simply from an abnormal exhaustibility of the respiratory center (not to be confused with diminished irritability). The center is active for a time, works against a gradually increasing difficulty, finally stops entirely, and begins its activity again only after the pause has to some extent recuperated its powers. It seems doubtful whether we can assume that such recuperation of the respiratory center occurs during the breathing pause, while the respiratory irritant persists. The laws of fatigue in the central nervous system are, however, so imperfectly understood that this objection to Rosenbach's explanation is not sufficient to make us reject it entirely. At all events it has the advantage of depending upon the same law that applies to the other organs—that periodic activity usually arises as a result of fatigue.

Most types of increased respiratory frequency (polypnea) depend upon an increased demand on the respiratory activity, and will therefore be discussed in the following section on Dyspnea. We should, however, mention the fact that increased frequency of breathing may arise from purely nervous causes, *e. g.*, in hysterical people and in certain cases of cerebral disease.

DYSPNEA

The term dyspnea applies to a large group of variations in respiratory activity, which, in spite of considerable diversity in detail, have this in common, that they serve to promote the object of breathing, *i. e.*, the proper oxidation of the blood, despite all kinds of obstacles. On this account the breathing of dyspnea is generally increased in frequency or in depth. The obstructions to breathing are, however, sometimes insurmountable, so that neither a frequent nor a deep type of breathing is possible, *e. g.*, in marked stenosis of the air-passages. Therefore increased breathing must not be considered absolutely the essential feature of dyspnea. The only definition which will apply clinically to all cases is that dyspnea is an increased respiratory exertion produced by obstruction to breathing or by increased demands upon the blood-oxidizing process. This does not coincide with the explanation frequently given, that dyspnea is identical with quickened breathing, which is unquestionably inaccurate from the clinical standpoint, for not every case of quickened respiration is dyspneal nor is the breathing quickened in every case of dyspnea. As we shall see, there are

types of dyspnea with quickened and others with retarded respiration. To conform with the definition cited above and to avoid any misunderstanding, it is advisable to apply the terms *polypnea* to quickened and *oligopnea* to retarded breathing.

The word dyspnea is, however, employed in still another sense, to express the subjective sensation of oppressed breathing experienced by patients with objective dyspnea. Ordinarily, subjective and objective dyspnea go hand in hand; but exceptions do occur. For under certain conditions, despite the presence of some obstruction which is responsible for an objective dyspnea, breathing may continue so satisfactorily that the patient does not experience any shortness of breath, because, owing to the modification of the respiratory movement, the aëration of the blood is accomplished as completely as ever. Again, despite a very pronounced objective dyspnea which is by no means adequate for blood aëration, as evidenced by the accompanying cyanosis, a patient may have become so accustomed to it (see p. 102) or his sensorium may be so benumbed that he has no appreciation of subjective dyspnea. It is a very benevolent provision of nature that in the death agony, where the breathing is difficult, the brain becomes, as it were, so narcotized by the carbon dioxid intoxication that it no longer appreciates the sensation of the struggle for breath. Conversely, the objective dyspnea may be almost or entirely overshadowed by the intense "air-hunger." Examples are the so-called "precordial terror" of melancholiacs, which, because the individual locates the sense of anxiety in the chest, we prefer to consider as a subjective dyspnea which is purely cerebral. Again, some nervously organized individuals will complain of a transitory desire to draw an extra deep breath; they have the sensation of dyspnea without any evidence of obstructed breathing. In other words, it is a purely cerebral phenomenon, of which they instinctively try to rid themselves by taking a long breath.

Hence it is important to differentiate sharply between objective dyspnea, *i. e.*, difficult and hence modified breathing, on the one hand, and subjective dyspnea, or the sensation of lack of air, on the other. Sometimes breathing modified by dyspnea is accompanied by subjective dyspnea, but at other times this is not the case.

Cyanosis, like subjective dyspnea, is not always proportional to the degree of objective dyspnea, for in one case the objective dyspnea may be effective in regulating the proper aëration of the blood and in bringing conditions back more or less to a normal standpoint, whereas in other cases this is not possible for the organism.

The occurrence of decided objective dyspnea without cyanosis is a clinical proof that the intensity of the respiratory movement does not depend exclusively upon the grade of aëration of the blood, but may be produced directly by some obstruction to breathing without the appearance of cyanosis. A similar proof is furnished by the dyspnea which follows physical exertion. This in no way depends upon an excess of carbon dioxid nor upon a deficiency of oxygen in the blood so long as the breathing and the circulation remain sufficient.

To aërate the blood properly under adverse circumstances the organism avails itself of an increase either in the frequency or in the depth of the respiration. With an increase in the depth of the individual breaths, the frequency may be either accelerated, normal, or slowed. There are, therefore, various types of dyspnea, but generally we find

that it modifies the normal breathing in that way which seems best adapted to meet the existing deficiencies.

In the following we shall characterize the kinds of objective dyspnea occurring in different diseases.

VARIOUS TYPES OF DYSPNEA

1. Dyspnea Caused by Painful Breathing.—Patients are not infrequently prevented from drawing a deep breath on account of the pain associated with each respiratory movement in certain pulmonary, and especially pleural, disorders, in affections of the intercostal muscles (rheumatism, trichinosis) and of the diaphragm and its vicinity (peritonitis). The breathing then becomes superficial, and to satisfy the demand, more frequent—in other words, dyspnea results. In this instance the obstruction is functional, not mechanical.[1]

2. Dyspnea Due to a Diminution in the Breathing Surface of the Lung or to a Mechanical Limitation of the Respiratory Excursions of the Lung.—The two factors ordinarily occur together. Under this heading are included all affections of the pulmonary parenchyma which lead to a diminution of the air content of the lung, *i. e.*, all sorts of pulmonary consolidation, as well as pulmonary edema; all conditions which limit the capacity of the thorax, such as pleuritic effusions, pneumothorax, intrathoracic tumors, lateral curvature, upward displacement of the diaphragm; further, all conditions which decrease the respiratory excursions, such as brown induration and emphysema (with regard to emphysema, see p. 97 et seq.), as well as paralyses and spasms of the respiratory muscles.

In any of the above conditions each breath aërates the lung less efficiently than normally, with a resulting dyspnea and increased frequency of respiration. Under some conditions the demand for air will be completely satisfied, so that in spite of the interference with respiration neither cyanosis nor any subjective sense of dyspnea ensues. Under other conditions the compensation is not always complete, especially when any increased demand for air arises, so that physical exertion will occasion cyanosis and a subjective sense of dyspnea.

If such an interference with breathing be unilateral, *e. g.*, consolidation or a pleuritic exudation, the dyspnea can be partially compensated by deeper breathing of the healthy side (vicarious respiration), as well as by the increased frequency of respiration.

(See p. 87 et seq. concerning local depressions of the thorax in this variety of respiratory interference.)

3. Dyspnea Due to General Circulatory Disturbances.—Noncompensated valvular lesions may be regarded as a type. Here the chief factor is the stasis or congestion, *i. e.*, the circulation is slowed and the blood accumulates in the veins, whether the difficulty affects the left, right, or both sides of the heart. As a consequence of the retarded current the different organs receive less arterial blood in a certain time and retain more venous blood; and since the respiratory center is also affected by this disturbance, more rapid and deeper breathing results.

The conditions become more complicated when the circulatory trouble originates in the left heart, because the congestion then includes

[1 A type of dyspnea associated with a remarkable slowing of the respiration is sometimes observed in pneumonia when the accompanying pleurisy excites intense pain with each respiration.—Ed.]

not only the general systemic veins, but also the pulmonary veins, thus adding another cause for dyspnea—namely, a marked distention of the pulmonary capillaries with blood. It was formerly assumed that this dilatation of the alveolar vessels impaired respiration by diminishing the amount of air in the lung. But this conception was shown to be incorrect by von Basch's experimental investigations upon pulmonary congestion, for he proved, on the contrary, that the lung overdistended with blood contains more air because the distention of the alveolar vessels also increases the circumference of the alveoli. Nevertheless, the process in question does impair respiration, because the lung, stiffened by the distention with blood, becomes more and more permanently fixed in the position of inspiration and expands but little. Pulmonary rigidity acts as a direct impediment to breathing (category 2) and increases the respiratory rate. If it be persistent, its effect is intensified by the formation of the so-called "brown induration."

In opposition to this mechanical theory of pulmonary rigidity we would emphasize the work of Krause, who found that, in spite of the engorgement of the lung, each respiratory excursion may even be increased, *i. e.*, the breathing may be deepened. In this case the author believes that the dyspnea is to be explained not by pulmonary rigidity, but by the fact that the respiratory surface of the dilated pulmonary vessels is relatively decreased in comparison with their contents.

When the lung is affected paroxysmally by pronounced engorgement with blood and rigidity, in disturbances of cardiac activity, the resulting attacks are named "cardiac asthma." This term is often wrongly applied to any kind of dyspnea which appears in heart disease. These paroxysms of cardiac asthma are brought on sometimes by exertion, sometimes by increased flow of blood to the lung in the recumbent posture, sometimes by altered innervation at the moment of falling asleep, and sometimes by entirely unknown causes.

Pulmonary rigidity and brown induration arise in mitral diseases, especially when compensation is good, *i. e.*, when the right ventricle does its work well. For this reason patients with a mitral lesion, despite good compensation, experience dyspnea, even with very moderate exertion.

As a further cause of dyspnea may be added the *bronchial catarrh* that almost always accompanies circulatory disorders.

4. Dyspnea Dependent Upon Obstruction of the Upper Air-passages.—Any obstruction in the large upper air-passages makes breathing difficult because it furnishes a resistance to the entrance of air and to the inspiratory pull of the respiratory musculature. The latter must therefore perform more work. It is evident that under these circumstances an increase in the rate of breathing would be not only very difficult, but also of little avail, while, on the other hand, simple reflection shows that slowed breathing would more readily overcome the obstruction. But to supply the requisite amount of oxygen the breathing must be deeper as well. And this is sometimes observed to be the method which patients adopt to overcome obstruction in the larger air-passages, but only when there is sufficient inspiratory power to overcome entirely the impediment in breathing, for by this method the lung is just as well ventilated in the unit of time as is the case under normal conditions. Lacking such power, the economy is obliged to depend more and more upon the less efficient means of increasing the frequency of the breath-

ing, which, of course, becomes superficial; but that it is always suited to the particular kind of mechanical obstruction is shown by the fact that the increased frequency is slight in comparison with the extent of the respiratory obstruction, for too frequent breathing would be of no avail. This peculiar type may be termed *dyspnea with a tendency to slowed breathing.* The frequency or the depth of the breathing preponderates, depending upon the relation between the stenosis and the respiratory power. This type is observed in stenosis of the pharynx from swelling of the tonsils; in retropharyngeal abscess; in true croup and pseudocroup; in edema and in spasms of the glottis; in paralysis of the abductors of the vocal cords; in stenosis of the larynx or trachea from tumors or foreign bodies; in obstruction of the trachea from external compression (goiter, aneurysm, etc.). If the stenosis be situated in one of the main bronchi, it will depend again upon the degree of obstruction whether the dyspnea is combined with slowed or accelerated breathing. If the lung upon the affected side can still be made use of, the dyspnea will be of the former type; but if the healthy lung must do almost all the work, the breathing will be rapid. In either case the economy selects the more advantageous method. Thus, in all the conditions in question the demand for air will be supplied and the subjective dyspnea and cyanosis avoided, unless, of course, the obstruction is too great.

When the obstruction in the upper air-passages is very considerable, and when, despite the changes in respiration resulting from the dyspnea, the lung can no longer completely fill itself with air again, the chest "pumps empty," so to speak. During inspiration an abnormally rarefied space is found in the lung, and the lateral flexible portions of the chest-wall, the epigastrium, the supraclavicular fossæ, and the suprasternal notch (jugulum) sink in under the influence of the external atmospheric pressure.

There is another cause for depression of the lower lateral chest regions in this form of dyspnea. As a result of the empty pumping, the vault of the diaphragm is not depressed with inspiration, but may even be sucked upward. Besides, as a result of the stenosis, the ribs cannot be lifted up by the diaphragmatic action (described by Duchenne, p. 88), and so the contraction of the diaphragm practically accomplishes nothing but drawing in its points of attachment to the ribs. This pathologic retraction of the lower lateral portion of the entire chest-wall must not be confounded with the purely physiologic retraction of the lower intercostal spaces in inspiration. (See p. 86.) The differentiation is easy enough. In the latter only the lower intercostal spaces along the line of the diaphragm are affected, and there is never any retraction of the ribs nor of the epigastrium. The retraction of stenosis is observed most distinctly in children because their chests are very flexible. It is very common in croup.

A peculiar stridor or a sort of whistling, due to the passage of air through a narrowed place, is a most characteristic accompaniment of dyspnea caused by stenosis of the upper air-passages. It is ordinarily heard much more distinctly with inspiration than with expiration. In laryngeal croup the stridor is due to the membrane covering the vocal cords. The inspiratory accentuation of the stridor is explained by assuming that, in spite of the inspiratory opening of the glottis, the vocal cords are not materially separated, and that, as a result of their slanting,

roof-like position, they are approximated still more closely, valve fashion, by the pneumatic tug of inspiration. Hence, the obstacle to inspiration is greater than to expiration. This explanation is probably correct for cases of laryngeal croup. Nevertheless, the same inspiratory increase of stridor is observed in other types of stenosis of the upper air-passages, where we cannot assume the result of any such valve-like effect in the larynx, *e. g.*, from obstruction either above or below the larynx (retropharyngeal abscess, goiter, etc.). The probable explanation of such cases is that the obstruction prevents the free ingress of air during the inspiratory effort at a moment when suction is exerted upon the surrounding parts by the external atmospheric pressure, so that the trachea is constricted below the sternum (inspiratory retraction of the jugulum, suprasternal notch). Therefore, any obstruction in the upper air-passages, even if not actually located in the larynx, acts much more effectually during inspiration than during expiration. In other words, the dyspnea is essentially inspiratory. Another factor may influence this inspiratory accentuation of the stridor. The velocity of the air-current in inspiration is much greater than in expiration, which is passive, depending upon the elasticity of the lungs and the thorax. The importance of this factor is shown by the fact that, as soon as patients with stenosis of the upper air-passages experience a sufficient increase in the respiratory obstruction to necessitate their employing the help of abdominal pressure, the expiratory stridor will become more marked, and may even outweigh the inspiratory stridor.

5. Dyspnea in Bronchitis.—The types of bronchitis which usually lead to dyspnea are chiefly those affecting the smaller bronchi. The dyspnea is caused by the stenosis of the bronchial lumen, due to swelling of the mucous membrane and to secretion. The stenosis affects so many places that ordinary breathing is insufficient and dyspnea arises.

This type of dyspnea varies with the conditions which prevail. If the stenosis affect only a small number of bronchi, simple increase of the breathing rate will usually overcome the difficulty. The stenosed areas are not benefited much by this method, but the uninvolved portions receive more air, and so the effect of the disturbance is compensated. This type of dyspnea then comes under our second heading. If the stenosis affect a large number of bronchi, the breathing varies according to whether the bronchial closure is quite complete and insurmountable, as in *capillary bronchitis* proper, or whether it is incomplete and still conquerable by the respiratory effort, as in *diffuse dry bronchitis of the medium-sized tubes*. In the former variety, of which capillary bronchitis is a type, the chief effect is again merely a diminution of the breathing surface, so that, as before, dyspnea with rapid respiration results. This, of course, only assists bronchial areas which still remain patent. In the second type, however, where we suppose that most if not all of the medium-sized bronchi are stenosed, although only moderately so (the so-called stenosing bronchitis in a more restricted sense), the respiratory effort must attempt to get a sufficient quantity of air through the constricted areas into the pulmonary tissue proper. This can generally be best accomplished by an abnormally deep respiration, very much as in stenosis of the upper air-passages, especially of the larynx. And just as in these cases, the respiratory accommodation and the frequency of the individual efforts will vary according to the amount of

obstruction as compared with the respiratory force available. In rare instances even a slowing of respiration may result. More frequently, however, we merely observe a certain tendency to retardation, in that the increase in rate does not correspond to the degree of constriction, and this increase is comparatively slight as contrasted with the amount of subjective dyspnea and cyanosis. The passage of air through these constricted areas is often associated here, as well, with a stridor, *i. e.*, a stenotic noise which may perhaps be heard at a considerable distance from the patient. This type of dyspnea in bronchitis presents, therefore, a prolongation of expiration and stridor, chiefly expiratory, and so can be distinguished from the other retarded type of laryngeal dyspnea, where expiration is of normal length and the stridor is chiefly inspiratory.

These two points of distinction, which are responsible for the application of the name expiratory to this type of dyspnea, require some further explanation. The prolongation of expiration is easily understood, because even under normal conditions expiration is longer than inspiration, and, of course, the increased resistance caused by the bronchial stenosis must be felt more during expiration, especially since the excitation of dyspnea produces, first of all, marked increase of the inspiratory power. To be sure, if the dyspnea be pronounced, the expiratory exertion must also be increased by the participation of abdominal pressure in the expiratory act, so that the lungs will then be emptied somewhat more quickly by the active expiratory compression of the thoracic contents than by the sole influence of elasticity. This extra abdominal pressure, however, will also compress the small bronchi still more; hence the prolongation of expiration as compared with inspiration, and the increase of expiratory stridor. Increased expiratory stridor may be present without the participation of abdominal pressure. For if the elastic retraction of the lung be interfered with by stenoses in the bronchi, the latter will be still more compressed by this elastic expiratory movement, just as by abdominal pressure. Hence, abdominal pressure is not absolutely necessary to account for the increased expiratory stridor. This compressing effect of expiration upon the finer bronchi is proved by the observation of the expiratory dyspnea in pneumothorax. (See p. 101.) All sorts of intermediate types occur between this type of retarded breathing with prolonged expiration and expiratory stridor, on the one hand, and the type in which the breathing is simply increased in frequency on the other. These types will vary according to the preponderance of bronchial stenosis or of the available respiratory power.

6. Dyspnea in Bronchial Asthma.—Bronchial asthma leads to a form of dyspnea with expiratory stridor, a so-called *expiratory dyspnea*, which differs from the expiratory dyspnea of stenosing bronchitis (see above) only by its occurrence in sharply circumscribed exacerbations or attacks. If the modern conception that bronchial asthma is due to a spasm of the bronchial muscles leading to a stenosis of the finer bronchi be true, the conditions correspond entirely with those in the last-mentioned form of bronchitis with diffuse moderate stenosis of the bronchi. This will apply so much the more if we regard asthma as a secretory neurosis associated with the production of viscid mucus. However, the author regards both these explanations of bronchial asthma as hypothetic and improbable, and for years has taught in his

clinic that the nervous element, undeniably responsible for the occurrence of attacks of bronchial asthma, is to be found simply in an increased irritability of the respiratory center.

Under all conditions a stenosing bronchitis is always present in bronchial asthma, and when the irritability of the respiratory center is increased from any cause, whether it be the bronchitic dyspnea itself, the nervous constitution of the patient, or an accidental excitation, the expiratory dyspnea due to the stenosing bronchitis becomes manifest or more pronounced simply because the quicker and deeper the breathing, the more potent become the previously mentioned mechanical causes of expiratory dyspnea. (See the section upon Dyspnea in Bronchitis.) With increased inspiration the lungs become more distended and the expiratory compression of the stenosed bronchi increases the expiratory dyspnea, especially when the expiration is of an active character. Any one may convince himself of the truth of this assertion by asking an asthmatic patient to breathe deeply at a time when there is little or no dyspnea present. The breathing will at once exhibit marked expiratory stridor and there is a demonstrable increase in the area of pulmonary resonance which differs in no particular from that observed in an asthmatic attack. In this experiment it is evident that neither spasm of the bronchial muscles nor an acute increase of secretion can be held responsible for the attack. The author's theory is also favored by the fact that the attack of bronchial asthma and the asthmatic disposition in general may be largely influenced by regulation of the respiratory excursion as well as by remedies which diminish the irritability of the respiratory center.

In bronchial asthma, therefore, there is a tendency to retardation of the breathing and particularly to a prolongation of the expiration. Inspiration and expiration are usually associated with stridor, but this stridor is more marked during expiration than inspiration. The absolute number of respirations may be diminished; or an increase in rate which would correspond to the amount of subjective dyspnea may be prevented. This depends upon the degree and the extent of the bronchial stenosis. In bronchial asthma, as in stenosing bronchitis, we may, therefore, observe either a diminished, normal, or increased frequency of respiration. The conditions are analogous to those in emphysema. (See next section.)

7. Dyspnea in Emphysema.—Pulmonary emphysema causes dyspnea because the lung is in a permanent condition approximating the inspiratory position, and because with inspiration and expiration it makes but small excursions from this position. Besides this, pronounced emphysema destroys numerous alveolar septa and their capillaries, thus diminishing the breathing surface very extensively. For this reason the dyspnea of pure uncomplicated emphysema is evidenced by rapid and superficial respiration. When the patient is quiet, the disturbance remains slight, but when some physical exertion makes extra demands upon the respiration, the dyspnea increases very decidedly. As a rule, patients with emphysema appear for the treatment of marked dyspnea only when this affection is complicated by a bronchitis (usually the dry variety). Consequently, in emphysema the same influences which we have just discussed in bronchitis tend to render the respiration now quicker and now slower. The tendency to retardation is very pronounced, because the bronchitis complicating the emphysema is usually

diffuse and produces a stenosis of most of the bronchi. The loss of elasticity in the emphysematous lung especially promotes a retardation of breathing and prolongation of expiration. But the dyspnea in emphysematous bronchitis is not always associated with a slowing of respiration, for the system will accommodate itself to the respiratory obstruction, with or without an increase of respiration, depending entirely upon the proportion between the extent of loss of elasticity in the lung, the degree of bronchial stenosis, and the amount of respiratory power. As a matter of fact, in the bronchitis of emphysema there is very often a certain amount of increase in the frequency of breathing. Still the subjective oppression outweighs the slight increase so decidedly that, unless we count, the impression is made that the respirations are slow, although actually they may be 20 to 25 a minute. In some cases this tendency to retardation leads to an actual diminution in the number of respirations; in other cases, only to a lack of any increase; in still another class of cases, to an increase in respirations which is but slight in proportion to the subjective dyspnea. Thus, the bronchial dyspnea of the emphysematous may be characterized as a dyspnea with a prolonged expiration and expiratory stridor (so-called expiratory dyspnea), and also with a more or less pronounced tendency to a diminution in the frequency of the breathing. These conditions are unchanged if, as is often the case, the emphysema is complicated with bronchial asthma.

8. So-called Uremic Dyspnea of Nephritis.—This exhibits no uniform symptom-complex. Only those cases should be designated as uremic asthma in which the breathing is characterized by prolonged expiration. In such cases we are led to suppose that a true bronchial asthma is present and that it is due to a uremic bronchitis associated with a uremic change in irritability of the respiratory center. (See p. 96 et seq.) Many dyspneic conditions in nephritis are, however, erroneously considered uremic. They depend rather more upon some cardiac disorder, upon the accompanying bronchial catarrh, or upon a beginning pulmonary edema, etc. Corresponding to the diversity in causation, these types of dyspnea vary decidedly in their character. It should be mentioned that dyspnea in nephritics is particularly frequent in combination with Cheyne-Stokes breathing. (See p. 88 et seq.) In reference to exaggerated breathing in uremia see Fig. 42, p. 100.

9. Febrile Dyspnea.—A febrile elevation of the body temperature is nearly always combined with an increase in respiratory frequency. Even the artificial application of heat to the body will increase the respiratory rate, so that it seems plausible that the irritation of warmer blood upon the respiratory center is responsible for the febrile rise of the respiratory rate.

However, the frequency of respiration in febrile diseases with exactly the same degree of temperature may differ widely, so that the nature of the toxin probably exerts some direct influence upon the respiratory center. The increased respiratory frequency in fever probably corresponds to an increased demand upon the metabolism. Therefore, according to our definition (p. 90), we are correct in speaking of febrile dyspnea as well as of febrile polypnea.

The respiratory frequency found with a certain degree of fever varies with each individual case. Experience shows that unless some respiratory complication exists, only the severe types of fever increase the respiratory frequency very noticeably. Fig. 30, the curve of an uncom-

plicated typhoid, illustrates the usual ratio between temperature and rate of respiration.

10. Anemic Dyspnea.—Exaggerated Breathing in Diabetic Coma.—Dyspnea occurs in anemia (oligochromemia) because the available amount of hemoglobin is so small that only the most complete aëration will be sufficient to supply the demand for oxygen. With no mechanical impediment to respiration, the organism can adapt itself very completely to the altered conditions. This is accomplished by a simultaneous increase in the frequency and in the depth of respiration. The resulting dyspnea produces a peculiar clinical picture, for the respirations are not only rapid, but also of maximum depth. This type is observed especially in pernicious anemia; rarely, however, in other disorders.

The same type of breathing is observed in diabetic coma,[1] and this phenomenon has been described by Kussmaul as "exaggerated breathing" (grosse Atmung). It is probably dependent upon the acidosis, as a result of which the alkalinity of the blood is diminished, the tissues are not sufficiently freed from carbon dioxid, and the respiratory center becomes abnormally irritable.

11. "Mixed" Dyspnea—Inspiratory and Expiratory.—Thus far we have been discussing the various factors which determine the different types of objective dyspnea. Two main types occur: (1) breathing with increased frequency and (2) slowed breathing with increased depth. In the former "mixed dyspnea" inspiration and expiration seem equally accelerated. In the latter, inspiration and expiration are affected differently; in some cases the inspiration, in others the expiration, appearing prolonged. One type is termed "inspiratory dyspnea," the other "expiratory"; because in the one it is principally inspiration, and in the other expiration, which is rendered more difficult. In this connection compare the paragraphs on the types of dyspnea in obstruction of the upper air-passages in bronchitis, in emphysema, and in asthma.

Inspiratory dyspnea can usually be distinguished immediately by inspiratory, *expiratory dyspnea* by expiratory, stridor, without necessarily estimating the length of the two phases of respiration. If the examiner be inclined to do this, he should remember that normally expiration lasts longer than inspiration.

12. Observations upon the Teleology of the Forms of Dyspnea.—The individual forms of dyspnea have been explained in the preceding sections as though the organism in each instance voluntarily selected that modification of respiration which was best adapted to the existing condition. Such an explanation might be objected to upon the ground that dyspnea has nothing to do with a modification of a voluntary movement and consequently that the demonstration of the utility of the modification does not furnish a sufficient explanation for the particular respiratory mechanism. In answer to this we would call attention to the fact that the demonstration of utility alone can by no means constitute an explanation, but that the explanation of the occurrence of the particularly appropriate phenomenon is given by the fact that the best adapted means offers the greatest chance of phylogenetic maintenance. Experience teaches us that this is true not only for voluntary action, but also for automatic movement, the utility of which may be demonstrated in almost any portion of the body. Pathologic automatisms also not infrequently arise through the medium of voluntary actions.

[1] Kussmaul, Deut. Arch. f. klin. Med., 1874, vol. iv.

GRAPHIC RECORDS OF THE FORMS OF BREATHING IN DISEASE (PNEUMOGRAPHY)

The graphic investigation of the respiratory movements in disease which was formerly neglected as compared with similar studies of the pulse has been recently elaborated, particularly by Hofbauer, and has furnished interesting results.

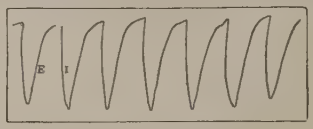


Fig. 39.—Respiratory curve of normal subject: *I*, Inspiration; *E*, expiration (reduced from Hofbauer).

A great variety of appliances may be employed to record the respiratory movements. In the Bern clinic we usually simply strap a cardiographic instrument, such as that of Jaquet's cardiosphygmograph (see Cardiogram), about the chest in such a manner that the "pelotte" of the air-chamber rests upon an area distant from the cardiac region instead of upon the apex-beat. The movements of the particular portion of the thoracic wall are transmitted by the air-chamber to the recording

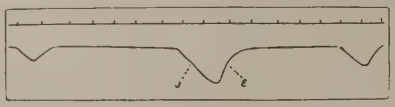


Fig. 40.—Respiratory curve in the exaggerated breathing of diabetic coma: *J*, Inspiration; *E*, expiration (reduced from Hofbauer).

appliance of the original or simplified Jaquet's cardiosphygmograph (see p. 126 et seq.) and traced upon a smoked strip of paper. Mackenzie has shown that a small funnel may be employed as a pneumatic appliance for recording the breathing graphically, just as is the case with the recording of the venous pulse. (See pp. 127 and 128.) The small funnel is held upon the jugulum or the supraclavicular fossa. By any of these simple procedures respiratory curves may be obtained which are

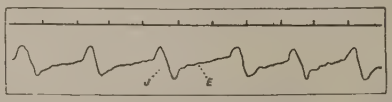


Fig. 41.—Respiratory curve in a case of recent pneumothorax: *J*, Inspiration; *E*, expiration (reduced from Hofbauer).

quite useful. If simultaneous records of other movements are not desired, the respiratory movement may be recorded without a special mechanism and without the employment of air-chambers with the ordinary Jaquet's sphygmograph or a similar appliance, if it be fastened about the chest in such a manner that the thoracic movements are transmitted to the pelotte. Respiratory curves obtained in this manner, like sphygmograms, may be differentiated by their height, by their steep-

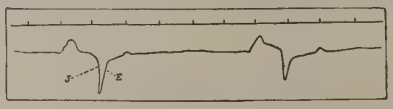


Fig. 42.—Respiratory curve in the exaggerated breathing of uremia: *J*, Inspiration; *E*, expiration (reduced from Hofbauer).

ness, and by the direction of their ascending and descending limbs. The graphic record of the height of the curve, however, has even a more limited value in a respiratory tracing than in a sphygmogram, because, with the same apparatus, it is dependent upon the area selected. Since the height of the curve influences the steepness of the limbs, we can base no inference upon the absolute steepness of the limbs of the curve (the size of the tangential angle). In the analysis of a pneumogram the only points from which conclusions may be drawn are: the comparison of the steep-

ness of the ascending and descending limbs of the curve, the duration of the ascending and descending limbs, and the form of the ascending and descending limbs in relation to their convexity or concavity and in reference to the change of direction of the curve (maximum, minimum, and changing points).

A critical employment of the curves demonstrates that pneumography is a useful addition to our methods of clinical investigation, and some of the typical curves obtained by Hofbauer have consequently been reproduced here.

Particular attention should be called to the prolonged expiration in the respiratory curve of pneumothorax depicted in Fig. 41. This is not so apparent in the course of an ordinary clinical investigation, since there is no expiratory stridor, no actual bronchial stenosis being present as in bronchial asthma or stenosing bronchitis, for example. It may be immediately recognized, however, if the duration of inspiration and expiration be timed with a watch provided with a second-hand. The prolonged expiration in pneumothorax, indicating, as it does, increased resistance to expiration, certainly proves the existence of a closed or valve pneumothorax. It is also of particular interest because it shows the compressing effect of expiration upon the finer bronchi, assumed in the author's explanation of the forms of expiratory dyspnea (see p. 96 et seq.), because in pneumothorax this is evidently the sole obstacle to expiration. It is apparent also that anomalies of respiratory rhythm, such as Cheyne-Stokes and meningitic breathing, furnish fruitful subjects for pneumographic records. Quite a number of interesting respiratory curves are given in L. Hofbauer's monograph.[1]

AUXILIARY OR ACCESSORY BREATHING; FORCED ATTITUDES IN DYSPNEA

In all types of dyspnea the economy ordinarily employs all the available aid to lighten the burden of the respiration. In this way a number of muscles are used for breathing which, under normal conditions, serve other purposes. These are the so-called accessory respiratory muscles, chiefly the scaleni, trapezius, levator anguli scapulæ, sternocleidomastoid, sternothyroid, thyrohyoid, serrati, and the pectorals. The last five mentioned muscles may serve as inspiratory muscles, their usual fixed attachment to the chest being made the mobile point, the other end becoming stationary.

We have already considered upon p. 23 how the erect posture facilitates the task of these accessory muscles (orthopnea), and the importance of constrained lateral positions with a unilateral obstruction to breathing. The abdominal muscles are the only ones employed as accessory muscles to expiration. Naturally they are chiefly active in expiratory dyspnea, but they may also be utilized to advantage in mixed and in inspiratory dyspnea to accelerate expiration and thus to facilitate a new inspiration.

If the dyspnea be very pronounced, various other accessory muscles to respiration may be called into play. Their activity is of certain diagnostic importance, although it must be acknowledged that they do not materially assist the respiration. The facial muscles of expression are examples. During inspiration they distend the openings of the mouth, and especially of the nose, to a maximum. The patient thus presents quite a characteristic and pitiful appearance. This dilatation of the alæ nasi is especially pronounced in small children with pneumonia. Such a maximal distention of the entrances to the respiratory tract may sometimes be of real value; but it ordinarily means that some effect of the vigorous respiratory stimulation has been transferred to related muscle groups.

[1] Semiologie und Differentialdiagnostik der verschiedenen Arten von Kurzatmigkeit auf Grund der Atmungscurven, Jena, Fischer, 1904. This monograph also gives the necessary references to the literature

RELATION OF OBJECTIVE DYSPNEA TO CYANOSIS AND TO SUBJECTIVE DYSPNEA; HABITUATION TO RESPIRATORY OBSTRUCTION AND TO DYSPNEA

Objective dyspnea serves to diminish both cyanosis and the subjective sense of dyspnea. This task is not always performed equally well. The more completely the dyspnea aërates the blood, the less danger to the individual; but cyanosis can only be entirely overcome when the obstruction to inspiration is slight. Wherever a marked obstruction occurs, some little—oftentimes considerable—cyanosis must persist. The economy then performs its functions with blood rich in carbonic acid and poor in oxygen, and the dyspnea only succeeds in preventing a progressive deterioration of the blood. In cases of chronic dyspnea the economy may become more or less accustomed to the cyanosis. This is evidenced not only by the relatively good maintenance of the other body functions, but also because the sense of subjective dyspnea, "air hunger," gradually and progressively disappears. Conversely, with the same degree of respiratory obstruction, the more quickly the latter develops, the more intense the subjective dyspnea.

Pneumothorax furnishes one of the most striking examples of the economy's power of adaptation to respiratory obstruction. After the sudden onset of the respiratory obstruction, both the objective and subjective dyspnea are at first very pronounced, but soon diminish. In pneumothorax this does not merely depend upon a simple adjustment of the economy to cyanotic blood any more than in other conditions. For in this type, as in many others, the disturbance itself is lessened by a number of complicated, compensatory factors which proceed especially from the circulatory system. This also becomes plain from the diminution of objective dyspnea. Among these compensatory factors is the increased production of red blood-corpuscles produced by dyspneic irritation of the bone-marrow, which, by increasing the hemoglobin supply of the body, enables the organism to meet its demands for oxygen even with an incompletely aërated cyanotic blood.

We need scarcely add that dyspnea with a slight degree of cyanosis suggests a far better prognosis than dyspnea with pronounced cyanosis.

SPIROMETRY AND PNEUMATOMETRY

Spirometry and pneumatometry, *i. e.*, the mensuration of the vital capacity and of the respiratory pressure variations in the upper air-passages, have not as yet acquired any great diagnostic importance. This failure is due to the great difficulties in technic and to the pronounced influence of practice in those examined. Readers who wish to study thoroughly this method of examination should consult textbooks upon physiology and several of the original works upon pneumatometry.[1]

The pneumoscope described by Bloch[2] seems to be the most useful for clinical purposes. Without determining the respiratory pressure manometrically, this instrument calculates the respiratory power by estimating the minimum diameter of a breathing cannula held in the mouth through which a sufficient quantity of air may be breathed. More accurate information of the respiratory mechanism can usually be obtained by pneumography (see p. 100 et seq.) and by directly measuring the thoracic excursions with a tape-measure than by spirometry or pneumatometry. (See p. 29 et seq.) Winternitz,[3] however, has recently advocated the employment of spirometry in pleuritic exudates to estimate the quality of the respiration.

[1] P. Donders, Zeit. f. rat. Med., N. F., 1853, vol. iii, p. 287 et seq.; Waldenberg, "Die Manometrie der Lunge, oder Pneumatometrie als diagnostische Methode," Berlin. klin. Woch., 1871, No. 45; Eichhorst, Deut. Arch. f. klin. Med., 1873, vol. xi, p. 268; Biedert, ibid., 1876, vol. xviii, p. 115; Rollet, ibid., vol. xix, p. 284; Neupaur, ibid., vol. xxiii, p. 481.

[2] Arch. de Physiol., 1897, p. 1.

[3] Med. Klinik, 1905, No. 45.

CHARACTER OF THE VOICE UNDER PATHOLOGIC CONDITIONS

Pathologic alterations in the voice arise partly from demonstrable disorders of the vocal organ proper (the larynx) and partly from other influences, either direct affections of, or disorders indirectly connected with, the respiratory apparatus. We shall mention here only such alterations of the voice as are of some diagnostic importance.

If the expiratory current of air does not make the vocal cords vibrate normally, the voice will be "*hoarse,*" *e. g.*, in all inflammations, ulcerations, tumors, or paralyses of the cords. A hoarse voice always indicates some affection of the larynx and necessitates a laryngoscopic examination. If combined with inspiratory dyspnea, hoarseness is very suggestive of laryngeal obstruction. It may, however, be due to some general condition, *e. g.*, the loss of the cords' normal tone in weak, cachectic patients. Again, it may result from a fit of violent coughing. Here a paresis of the tensors of the cords is caused by the marked stretching of the cords during the glottic closure which precedes the cough. The hoarseness in phthisis, therefore, does not always mean an ulceration or even a catarrh of the larynx or cords.

In hysterical aphonia the voice is frequently lost without preliminary hoarseness; whereas a similar loss of voice is always preceded or introduced by hoarseness if the aphonia be due to anatomic changes in the larynx. This is a point of some diagnostic importance.

The voice may acquire a nasal twang as a result of alterations in the conditions of resonance in the mouth or nose. We distinguish a closed nasal voice from an open nasal voice. The former is observed when the nasopharynx or the nasal cavity itself is obstructed by any pathologic products, such as tumefactions of the mucous membrane, polypi, adenoids. The latter, the "open nasal voice," is observed when anything prevents the normal closure between the nasal cavity and the mouth, *e. g.*, palate paralysis, cleft palate, syphilitic affections of the palate, etc.

Aphonia (lack of voice) results either from an inability to approximate the vocal cords or from a prevention of the normal vibration. It may be preceded by hoarseness.

The voice is, moreover, very dependent upon the general condition and upon the thoracic organs. Patients who are very ill usually have a weak voice, corresponding to their general muscular weakness. In diseases of the respiratory and circulatory organs the voice is affected by the disturbed respiratory excursions and by the various sorts of dyspnea. In many patients with heart disease the voice (*i. e.*, the cord tonus) is a very delicate indicator of the condition of their general circulation—it becomes weak and feeble when they fail, and full and sonorous when they improve. In painful affections of the lungs or pleura and in peritonitis the voice becomes characteristically feeble, soft, and often broken. Cholera patients speak with a "toneless" voice (vox cholerica), and the moribund with a faint, scarcely audible voice. Further reference will be made to these and similar points in the section on Auscultation (bronchophony).

COUGH

A cough consists of a single or of a consecutive series of explosive expiratory movements produced by abdominal pressure, which result in overcoming the preliminary closure of the glottis. It is a very important *reflex act*, serving the purpose, on the one hand, of expelling any foreign bodies which may have become lodged in the respiratory passages, and, on the other hand, of expectorating any material which may have accumulated there from some pathologic process, *e. g.*, bronchial or alveolar secretions, effused blood, pus which has perforated into the bronchi, disintegrated necrotic or tuberculous lung material, etc. A cough may be excited from various places in the body. The commonest type of cough is one in which the reflex arises from the region supplied by the sensory branches of the vagus. Experimental investigations have shown (especially Nothnagel's) that irritation of the laryngeal mucous membrane *above* the vocal cords produces spasmodic closure of the larynx, but no cough. Coughing will, however, be induced if the irritation affect the parts *below* the vocal cords. Under pathologic conditions, however, there is no doubt that affections of the pharynx and nasopharynx may produce cough. The most sensitive areas, as shown in Nothnagel's experiments, are the interarytenoid mucous membrane and the region of the bifurcation of the trachea. Coughing may also be excited from any other part of the tracheal, as well as from all parts of the bronchial, mucous membrane, but not from the pulmonary parenchyma proper.

Experimental results do not agree as to whether a cough can be excited directly from the pleura; but it seems probable, judging from experience with individuals whose pleura has been opened. From a teleologic standpoint such experience is of no value, since the results obtained may be explained by a pathologic radiation of the excitation. Upon the whole, the susceptibility to cough-exciting influences seems to diminish as we pass from the larynx toward the finer bronchi, because, from apparent reasons (the diminished expulsive power of coughing, the greater effectiveness of the ciliary movements), coughing is of less teleologic importance for the deeper respiratory passages than for the upper ones. This is in accord with the fact that unusually violent paroxysms of coughing indicate, with a fair degree of probability, the larynx and the trachea as the site of origin.

These are the most important sources of the excitation of coughing, but there are other less common ones. In some individuals coughing may be produced by irritation of the pharynx or of the base of the tongue, or occasionally of the esophagus. Coughing has been observed very exceptionally to result from tickling the external auditory canal (auricular branch of the vagus) or from manual pressure upon the spleen or liver. Some people cough as soon as their feet become cold or whenever their body surface is exposed. This suggests the therapeutic value of warm clothing in diseases complicated with a cough. This phenomenon, which possesses no teleologic explanation, probably comes under the head of the pathologic radiation of irritations from one nerve area to another. The existence of a stomach cough is very doubtful, although the lay public speak of it very frequently. Cough has not as yet, however, been experimentally excited from the stomach, and the so-called stomach

cough, which is so common in drunkards, can probably be most satisfactorily explained by assuming that an affection of the pulmonary passages [or pharynx.—Ed.] is combined with the stomach disorder.

Nervous Cough.—The so-called nervous cough merits a few words. We cannot deny the possibility of a nervous cough if we consider that a cough can be produced by an abnormal excitability anywhere in the course of the coughing reflex arc. When such reflex excitability is accentuated sufficiently, even physiologic irritants may cause a cough. As a matter of fact, a purely nervous cough is a very rare occurrence, and should only be diagnosed as such when it is observed in an exquisitely nervous or hysteric person, and when at the same time it differs decidedly from the ordinary type of cough. Under no circumstances is such a diagnosis justifiable from exclusion, *i. e.*, because the cough is the only sign of disease of the respiratory tract that can be made out from physical examination. It is well known that a cough frequently precedes all other signs of tuberculosis by weeks, often by months. (See under Barking Cough.)

Much more frequent than a purely nervous cough is one which is disproportionate to its cause (*i. e.*, secretion or inflammatory irritation of the air-passages), on account of an abnormal excitability of the coughing reflex. In such cases soothing remedies afford great relief.

On account of the rarity of other causes, a cough is usually an important symptom for the recognition of some state of pathologic irritation in the region of the respiratory branches of the sensory vagus. This irritation is in many cases produced by the accumulation of secretion in the air-passages. Experience teaches us that a cough caused by accumulation of secretion differs from the other types of cough. This difference is often appreciated by the laity. Its task, which is generally fulfilled, is to remove the secretion. It thus acquires a peculiar ring, recognized as a combination of the noise of the cough explosion with the noise of the moving secretion. (See later Râles, Rattling.)

Such a cough is called a **moist** or **loose cough** as contrasted with a **dry cough,** in which either the secretion is too tenacious to be set in motion or no secretion exists. The acoustic distinction between a moist and a dry cough is of considerable diagnostic importance, because the secretion is by no means always expelled from the mouth by the cough and so appreciated by the patient and the examiner, but very frequently after leaving the larynx is unconsciously swallowed.

There are certain other important peculiarities in a cough which may point to the cause of the disease.

The **peculiar rough barking cough** observed in simple and croupous laryngitis is characteristic of swelling without marked ulceration of the vocal cords. Here the voice may be clear, but it is usually very hoarse or aphonic. The barking tone is probably due to the swelling of the false cords which aid in closing the glottis. A similar barking is sometimes observed in the cough of hysteric individuals. Here the laryngoscopic examination proves that it is due to some abnormal innervation without any swelling. With a certain amount of practice one can really cough with a bark by adding phonation to the cough impulse. Like most other hysteric phenomena, it can be reproduced voluntarily. If not associated with swelling of the larynx, a barking cough suggests its hysteric nature.

If the margin of the vocal cords be irregular from deposition of

secretion or from ulceration, the cough is equally rough but not barking, and the voice is hoarse. If the closure of the glottis be imperfect on account of marked ulceration of the cords or on account of paralysis of the approximating muscles, or, if there be paresis of the expiratory muscles or general debility, the cough is noiseless. This peculiarity is observed in phthisis of the larynx, in paralysis (bulbar paralysis, myelitis), in any patient who is weak or severely ill. If a patient be unable to approximate the glottis perfectly, he may instead be compelled to close the mouth for the purpose of coughing, and then the resonation from the distended buccal cavity will furnish a very hollow ring to the cough. Such a hollow ringing is so generally observed in advanced phthisis that even the laity appreciate its prognostic significance.

A **hacking cough** consists of a series of very weak, frequently repeated coughing explosions. It is to be attributed to the mildness of the irritant, which in these cases is usually continuous and is not dependent upon any great amount of secretion. A hacking cough is most commonly observed in chronic catarrh of the upper air-passages, in pharyngitis and laryngitis, and especially in beginning pulmonary tuberculosis; hence its importance.

Conversely, **violent coughing paroxysms** are observed in acute, intensely irritated conditions of the air-passages from acute inflammations or from foreign bodies in the air-passages; in "swallowing the wrong way"; in affections of the air-passages associated with a profuse secretion, especially where cavities or bronchiectatic dilatations empty themselves periodically (see p. 24), and finally in *whooping-cough*. In the last-mentioned affection we may attribute the cause to the abundant production of glairy mucus and to the increased irritability of the nervous coughing mechanism. The "*whoop*," so important for diagnosing this disease, is a resounding crowing or whistling inspiration, combined with a spasm of the glottis, and separates individual groups of coughing attacks. The glottic spasm is evidently due to some radiation of the irritation from the coughing center to the neighboring structures of the central organ, and depends merely upon the intensity of the irritation. During violent coughing paroxysms of other diseases we sometimes observe resonant inspirations very much like this whoop, but so rarely that the "crowing inspiration" is the most important diagnostic sign of whooping-cough.

Vomiting sometimes complicates very intense coughing paroxysms; it is due to the central diffusion of the irritation.

Hemorrhage into the skin or mucous membranes, unconsciousness, or even epileptoid convulsions may be produced by the general venous congestion due to compression of the intrathoracic veins.

A physician must be very careful in taking the history of a patient in regard to coughing. So long as the cough or the hacking causes neither inconvenience nor discomfort, patients, especially the phthisical, persistently deny that they cough, even when the physician hears the hack himself. By imitating the sound and movements of such a "hack," a physician can sometimes get the patient to acknowledge that he does "hack," but that he never considered it a cough.

It must, however, be acknowledged that some cases of phthisis or bronchitis with very intense inflammation of the lungs occur without any cough or even a "hack." Here the secretion is probably brought up to the vocal cords by the motion of the cilia of the mucous membrane, and is then removed by "clearing the throat." If, as frequently happens, the secretion be swallowed, the patients neither cough nor expectorate.

LOCALIZED PROMINENCE OF THE CHEST IN COUGHING

As a result of the marked positive pressure and variations in the chest interior which are combined with the act of coughing, certain pliable portions of the thorax may be pushed forward at the commencement of the coughing spell in quite a remarkable way. If the glottis be closed, expiratory pressure distends the upper part of the chest chiefly, because the expiratory power fixes the lower thoracic aperture. In coughing, therefore, we generally observe a bulging forward of the upper intercostal spaces and apices of the lungs. Such bulging is especially prominent in emphysema, because the pulmonary resistance is impaired. The portion of the lung situated above the level of the clavicles shows an increase in volume, so that during a cough in emphysema we frequently notice that large swellings are produced above the clavicles. This phenomenon should not be confounded with the distention of the jugular veins during a cough, which is also oftentimes quite pronounced (p. 192 et seq.). If the lung tissue be infiltrated and shrunken, coughing will evidently not produce such an inflation. Hence a careful inspection of the supraclavicular fossæ sometimes furnishes important conclusions as to the condition of the apices in beginning tuberculosis.

PALPATION, SPHYGMOGRAPHY, AND SPHYGMOMANOMETRY OF THE ARTERIAL PULSE

Examination of the arterial pulse is of great diagnostic importance because it informs us of many things, such as the cardiac innervation, the force of the heart, the blood-pressure, and the condition of the peripheral arteries, and sometimes suggests the existence of valvular diseases of the heart or of fever. Many individual peculiarities must be considered and various methods employed to recognize them.

The commonest method and the one employed almost exclusively by practitioners is manual palpation of the arterial pulse.

Sphygmography, sphygmomanometry (tonometry), and sphygmobolometry are less used. Inspection and auscultation of the arterial pulse are much less important.

PALPATION OF THE PULSE

Any superficially placed artery may be utilized for the purpose of palpation; but we nearly always choose the same vessel, so as to have a certain uniform standard, experience, and practice in judging of the pulse. On account of its accessibility, the radial artery is usually selected. It is palpated between the styloid process of the radius, or the tendon of the supinator longus and the tendon of the flexor carpi radialis. An anomalous position of the artery or of the tendons will, of course, necessitate our trying another place. In doubtful or difficult cases the two radials should be compared, so as not to attribute erroneously some abnormality really due to local causes, to an alteration in the entire circulation. One radial not infrequently seems smaller than the other, whereas in reality it is merely a small branch which lies in the

ordinary place of the radial, the main trunk taking some abnormal course. Sphygmographic records have been employed to analyze carefully the differences in the pulses of the peripheral arteries, dependent upon their situation above or below an aortic aneurysm and upon whether or not the origin of the artery is narrowed (particularly common in aneurysms, Ziemssen). (See p. 152 et seq.) Such differences can also be appreciated by comparative palpation of the accessible arteries.

In palpating the pulse the index-finger is usually pressed upon the artery with a varying amount of force. When a certain amount of pressure is exerted, the artery is found to expand and to lift the fingers with every heart-beat, and it is this lifting which is known as the pulse. It must be noted that under normal conditions a certain pressure of the palpating finger is necessary for a distinct perception of the pulse, because Marey has shown (La circulation du sang, 1881) that the increase in caliber of the arteries with the pulsation is so slight that the pulse of a vessel as large as the abdominal aorta is scarcely perceptible if the outer surface of the artery be simply touched instead of pressed upon. We may consequently state that if the pulse be palpable without pressure, the pulsations will usually be visible (jumping arteries), and the condition present is one of abnormal volume or celerity of the fluctuations in [blood] pressure.

Palpation with one or two fingers is sufficient to determine the frequency and the rhythm; but we need three fingers for judging the form and celerity of the pulse-wave and the height of the blood-pressure.

CHARACTER OF THE ARTERIAL WALL

Palpation of the arterial wall permits us to determine whether arteriosclerosis is present or not, and whether the pulse-wave is modified by any factors in the wall itself.

The most important thing to determine is the amount of elasticity or rigidity and the thickness of the wall of the arterial tube. This can be most effectually determined by rolling the artery back and forth under the finger and by running the finger along its length, at the same time being careful to prevent the influence of the blood-current by compressing the vessel with another of the fingers. The artery is *soft*, *thin-walled*, and *elastic* in young and healthy individuals; but in *arteriosclerosis* or where the blood-pressure is permanently raised by an increase of the vasomotor tonus (chronic nephritis, lead-poisoning, plethora) we can often distinctly appreciate the *increased resistance* and thickening of the walls. The tortuous character of the artery so frequent in these conditions is caused by a definite elongation. At the same time some arteries may be tortuous without any arteriosclerosis, *e. g.*, the temporal arteries. The deposit of lime in the wall, which is observed in very pronounced cases of arteriosclerosis, can be felt very distinctly as rough, hard irregularities. Arteriosclerotic rigidity with even less marked changes, however, may usually be distinctly differentiated by its irregularity from the uniform hypertrophy of the arterial wall in chronic nephritis and other conditions of permanently increased blood-pressure. Although palpation is diagnostically important in determining the existence of arteriosclerosis of the peripheral arteries, it does not necessarily show whether the aorta, coronary arteries,

or other deep-seated vessels are normal or not. The arteriosclerotic changes may be very unevenly distributed, and the radial artery is one which shows no marked predilection for the changes incident to a generalized arteriosclerosis. Therefore, to demonstrate arteriosclerosis we should palpate as many as possible of the superficial arteries.

A persistently high-tension pulse is one of the most reliable indications of diffuse arteriosclerosis when the examination shows no other cause for it (nephritis, plethora, dyspnea); but even without high tension an extensive arteriosclerosis may exist; and the absence of high tension or rigid arteries is not sufficient evidence to exclude it definitely, especially in the case of the aorta and coronary arteries. On the other hand, proof of the existence of arteriosclerosis is essential although, unfortunately, many physicians erroneously diagnose this arterial change by a process of exclusion, merely because they are at loss to account otherwise for the existence of circulatory defects. Such a course is not justifiable even in case of elderly individuals, for all persons beyond a certain age do not necessarily exhibit arteriosclerosis; nor are arteriosclerosis and age actually identical conceptions. From an ethical standpoint, it is even more deplorable that any individual suffering with a circulatory disturbance not attributable to a valvular lesion should be alarmed by an immediate diagnosis of arteriosclerosis or arterial calcification.[1] The greater number of the maladies which are now hastily diagnosed as arteriosclerosis are nothing else than myocarditic or neurocarditic affections which it may be quite possible to arrest or cure. Bäumler rendered a great service when he called attention to the faulty routine diagnosis of arteriosclerosis and also pointed out that it not infrequently happens that localized arteriosclerosis is present in the extremities most used (particularly in the arms), and that such changes are of but little importance to the general circulation.

CHARACTERS OF THE PULSE

FREQUENCY OF THE PULSE

The pulse frequency (*i. e.*, the number of beats in a minute) is estimated by counting the radial pulse. It is advisable to count an irregular pulse for at least one minute and then to repeat, for otherwise the count may not be accurate. If repeated counts furnish different figures, the extremes should be noted.

A great many influences affect the frequency of the pulse physiologically, so that it is advisable to estimate the rate under conditions which are as nearly alike as possible, or, in case this cannot be done, to make allowance for the action of these influences in forming an opinion. In sensitive people any mental excitement whatsoever decidedly influences the pulse-rate. The physician's entrance is enough to cause a marked rise in the pulse, so that at the bedside it is advisable to delay counting the pulse until after conversing with the patient for a while.

Any bodily exertion or movement increases the pulse-rate. After running, gymnastics, fencing, or mountain-climbing the rate may be very greatly increased and still be within physiologic limits. Even the quieter motions in bed, voiding urine, or evacuating the bowels, materially increases the pulse-rate in very sensitive or very ill patients. After moderate activity the increase in rate soon subsides, but after prolonged, fatiguing exertion it may persist for some time. The pulse-rate, furthermore, depends upon the position of the body. After lying down, sitting up increases the frequency; so does standing up after sitting. This rise may be only transitory, due to the muscular exertion attendant upon the change of position, or to some extent permanent so long as the position is maintained.

[1] The popular and unscientific expression "calcified arteries," which has alarmed many a layman possessing an encyclopedia, has no basis in fact, since calcium salts are very often absent in arteriosclerosis and usually play an entirely subordinate rôle.

Guy found that in fasting, healthy men who had previously rested the pulse-rate was 66 to the minute while prone, 71 while sitting, and 81 when standing.

Ingestion of food increases the pulse-rate for several hours during the period of digestion, the amount of increase varying according to the quantity of food. The daily variations of the pulse are only partly due to the influence of the meals; for daily variations approximately parallel to the daily variations of temperature are observed even in fasting individuals. They usually amount to only a few beats.

Generally speaking, a high blood-pressure produces a slowing of the pulse, a low blood-pressure an increase in its rate. There are, however, many exceptions to this rule, although it undoubtedly possesses some teleologic importance. Marey attributes the increased pulse-rate in standing up as contrasted with lying down to the difference in blood-pressure. This, he believes, is higher in the recumbent posture.

[Meylan's blood-pressure determinations in the vertical and horizontal postures in a large number of students at Columbia University, my own in a series of school boys [1] and in many healthy and diseased adults, have convinced me that Marey's explanation and his premise upon which it is based are both incorrect. In general, an athlete in good training shows a slow pulse in the recumbent posture, and its frequency increases but a few beats a minute upon standing. The systolic blood-pressure, however, is apt to be 5 to 15 mm. higher in the erect than in the recumbent posture. Meylan regards the reverse (recumbent pressure greater than erect pressure) as an indication of physical or circulatory weakness. So far as they have gone, many of my observations suggest the same conclusion.—Ed.]

Respiration usually influences the pulse-rate; during inspiration it is increased, during expiration diminished.

Coughing or Valsalva's experiment produces a marked increase in the pulse-rate. In the latter the increased frequency persists longer than the increased intrathoracic pressure.

The time of life has a very distinct influence upon pulse frequency. Rollet [2] quotes the following figures, collected from various observers, as averages:

Age.	Pulse-beats to minute.	Age.	Pulse-beats to minute.
End of fetal life	144–133	10th to 15th year	91–76
Newborn and 1st year of life	143–123	20th to 60th year	73–69

Vierordt [3] gives the following detailed table for childhood:

Age.	Pulse-beats a minute.	Age.	Pulse-beats a minute.
1 year	134	7– 8 years	94.9
1–2 years	110	8– 9 "	88.8
2–3 "	108	9–10 "	91.8
3–4 "	108	10–11 "	87.9
4–5 "	103	11–12 "	89.7
5–6 "	98.0	12–13 "	87.9
6–7 "	92.1	13–14 "	86.8

The pulse-rate generally diminishes with the advancing years until the age of sixty, after which time it begins to increase slightly. Sex also has some influence. According to Guy, women average 7 to 8 beats a minute more than men of the same age. In individuals of the

[1] Potter and Harrington, Jour. Amer. Med. Assoc., vol. liii, No. 24, p. 1957.
[2] Hermann: Handbuch der Physiologie, vol. iv, 1.
[3] H. Vierordt: Daten und Tabellen, Jena, G. Fischer, 1888.

same age and sex the pulse-rate varies according to the height; it is slower in tall than in short persons.

Sometimes the pulse count at the wrist is less than over the heart. In such an event the latter must be the accurate measure of the heart's frequency, and we naturally conclude that the cardiac power has become affected, so that some of the pulse-waves are not transmitted to the peripheral arteries. Such an omission of individual beats makes the pulse sequence irregular, so that the examiner then turns to the heart. If the radial pulse be perfectly regular, we should not think of the existence of any difference between it and the heart-beat unless only some of the beats are strong enough to be transmitted to the radial artery, such as in pseudobradycardia (see p. 113), pulsus alternans and bigeminus, heart bigeminus, hemisystole, systolia alternans (see later sections upon the Modern Analysis of the Irregular Pulse and upon the Cardiac Impulse).

The pulse frequency, like the body temperature, can be conveniently represented upon a chart in the form of a curve. The variations of both can thus be very accurately compared at a glance.

Increase of Pulse Frequency; Tachycardia; Pseudotachycardia.—*Fever* is one of the most common causes of an accelerated pulse-rate (tachycardia). The temperature and the pulse-curve in fever usually run parallel. Liebermeister estimated that the pulse frequency was increased by about 8 beats for every degree of temperature. So long as pulse and febrile disturbance run parallel in this way, such a harmonious preservation of the functions may be regarded as relatively favorable. On the other hand, the more the acceleration of the pulse exceeds the elevation of temperature, the graver the prognosis, because too rapid a pulse-rate usually means some serious damage to the circulation, either to the heart or to the vasomotor system. If the patient be resting quietly, a pulse of 140 to 160 in fever is always of grave significance. Under various conditions of fever the pulse frequency and the temperature may follow an entirely different course. Such a divergence of the curves is of very great diagnostic importance. A high temperature with a slow pulse is observed chiefly in *febrile brain diseases*, in which the pressure upon the brain is responsible for the slowing of the pulse, as in *tuberculous meningitis* (Fig. 43); again, in a *combination* of a *febrile disease* with a *cardiac disturbance* which causes bradycardia (adiposity, sclerosis of the coronary arteries, myocarditis). The converse, a high pulse-rate with an abnormally low temperature, is characteristic of the symptom-complex of acute circulatory weakness included in the name *collapse* (Fig. 38).

There are numerous other exceptions to this rule of parallelism of the two curves, although most of them are less pronounced than the examples just cited, *e. g.*, in typhoid fever the pulse frequency is notoriously moderate as compared with the height of the temperature (Fig. 30). This peculiarity is often serviceable in differentiating typhoid fever from acute miliary tuberculosis or septicopyemia. For in the last two mentioned the pulse-rate is almost always accelerated out of proportion to the rise of temperature. Conversely, in pulmonary tuberculosis a very rapid pulse-rate is frequently observed with only a moderate rise of temperature or even with no rise at all. Yet the rectal is often unexpectedly higher than the mouth temperature. Children usually exhibit a relatively rapid pulse-rate with fever.

A rapid pulse-rate is, furthermore, found in affections of the heart or of the nerves. Valvular diseases in the stage of disturbed compensation, endocarditis, pericarditis, dislocation of the heart by processes in its vicinity which limit the space, exophthalmic goiter, nervous palpitation, nervous tachycardia—all of these diseases are or may be associated with a more or less considerable increase of the pulse-rate, to a certain extent proportional to the severity of the affection. Very imperfect explanation has been found for the cause of the increased pulse-rate in these cases. Mackenzie[1] has shown that the symptoms of the so-called paroxysmal tachycardia are probably due to an enormous accumulation of extrasystoles. The sphygmograms of markedly accelerated pulses corroborate his view in that normal pulse-periods

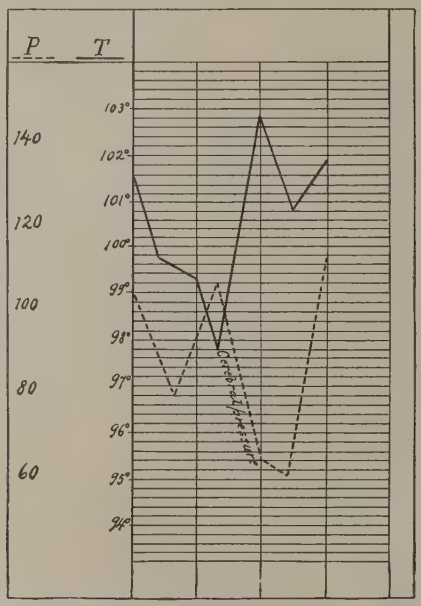


Fig. 43.—Relation of temperature and pulse frequency in tuberculous meningitis.

of varying length appear frequently, to which the accelerated pulse holds the relation of true extrasystoles. (See p. 154 et seq.) The undoubted occurrence of groups of extrasystoles in addition to the attacks of pronounced and long-continued tachycardia also favors this conception.

An increased pulse-rate also occurs combined with all sorts of pain. Under some conditions not yet understood the reverse at times occurs, *i. e.*, a slowing of the pulse. (See p. 113.) The reflex influence upon the cardiac nerves is the probable cause in both cases.

Atropin and alcohol are the two most important of the numerous poisons which accelerate the rate of the heart.

Not infrequently, under pathologic conditions, the acceleration of

[1] The Study of the Pulse, 1902, p. 124, et seq.

the pulse due in a healthy individual to physiologic influences (p. 109 et seq.) may reach an excessive degree so far as duration and intensity are concerned. This always points either to some damage to the heart itself or to its nervous mechanism. Thus, in chlorotics or in other weakly individuals even very slight exertion (stair climbing) will greatly increase the pulse-rate; and this increase is usually associated with the subjective sense of palpitation of the heart and of dyspnea. This phenomenon is of great diagnostic value from a functional standpoint. If dicrotism be misinterpreted as a pulsus bigeminus or alternans, as might happen in Fig. 63, p. 142, we could speak of a pseudotachycardia.

Diminution of the Pulse-rate (Bradycardia; Pseudobradycardia).—A noticeably slow pulse (bradycardia) does occur, although rarely, as an individual, non-pathologic peculiarity in a healthy person. A very pronounced slowing of the rate, to as low as 20 or less beats to the minute, is observed pathologically in certain diseases of the heart muscle, especially in the *fatty infiltrated heart* and in *sclerosis of the coronary arteries*. A greater or lesser degree of retardation is sometimes observed in *compensated aortic stenosis*. *Cachectic individuals* usually exhibit not only a low temperature, but also a slow pulse-rate (carcinoma of esophagus, etc.). Similar results are observed in convalescence.

A temporary slowing of the pulse (to a little below normal) is often found in acute febrile diseases after the crisis. When, despite the critical drop of temperature, the pulse remains high, there is always reason to suspect a "pseudocrisis." (See Fig. 29.) In certain painful affections (*e. g.*, gall-stone colic, lead colic), unless fever be present, a slowing of the pulse is more frequently observed than an increase. Icterus often produces retardation, due to the toxic action of the biliary salts. This, however, usually disappears when the jaundice is prolonged, either because the heart becomes accustomed to the intoxication, because the production of the biliary salts is diminished, or because their elimination is more complete. The slowing of the pulse in acute cerebral pressure is of particular diagnostic importance (meningitis (Fig. 43), fracture of the skull). Unless acute exacerbations occur, chronic cerebral pressure usually does not cause any slowing of the pulse. *Shock* sometimes causes an excessive slowing of the pulse. Rapid emptying of peritoneal or pleural effusions sometimes diminishes the pulse-rate.[1] Some drugs (digitalis, etc.) produce a slowing of the pulse.

In arrhythmia, when only the larger pulse-waves are palpable in the peripheral arteries, it is natural to assume erroneously that the pulse is slowed. The error will be disclosed by auscultation of the heart and palpation of the apex-beat. It goes without saying that such a control is necessary with every irregular pulse. It is not so well known that even with a regular pulse every bradycardia should be similarly controlled. As a matter of fact, there is such a thing as rhythmic pseudobradycardia, in which there is a decidedly slowed pulse in the peripheral arteries, while palpation and auscultation of the heart disclose the double pulse frequency. The phenomenon usually depends upon the existence of bigeminus (see Fig. 60, p. 138, and Fig. 76 *a*, p. 151), in which the second pulse (extrasystole) is not sufficiently recorded in the peripheral pulse-wave to appear as an independent pulse (see Fig. 153, "apparent

[1] [Capps and Lewis (Trans. Assoc. Amer. Phys., 1907, p. 635) have found that two types of reflexes result from thoracentesis in the presence of an inflamed pleura: (1) A cardio-inhibitory type, manifested by a slow intermittent pulse with a great difference between systolic and diastolic pressures; (2) a vasomotor type, manifested by a steady fall in blood-pressure without a marked difference in systolic and diastolic pressures, and by a pulse that grows steadily weaker until it cannot be felt.—Ed.]

bradycardia," in the section Recording the Cardiac Tones, p. 312.) With these pseudobradycardias may also be included the phenomena described at p. 159 et seq., in which the auricles (or the right auricle) beat more frequently than the ventricles, whether it result from a conductive disturbance or from a complete dissociation of auricle and ventricle (Stokes-Adams' disease; see also Cardiac Impulse: Double Beat of the Heart). Most excessive bradycardias in cardiac patients probably have some such special genesis which may frequently be determined by an analysis of the radial and venous pulse-curves. (See p. 157 et seq.)

PULSE RHYTHM

Under normal conditions the pulse is regular or rhythmic, *i. e.*, the individual pulse-waves follow each other at equal intervals of time. Only slight transitory deviations from such regularity come within physiologic limits, and then principally under conditions which modify the pulse frequency as well. More pronounced irregularities of the sequence of beats, or *arrhythmia*, are probably all pathologic, and indicate either some distinct lesion of the heart or some purely functional disturbance of its activity, such as occurs in all sorts of conditions, with or without cardiac weakness.

According to Mackenzie, over one-half of multiparæ exhibit during pregnancy disturbances of the pulse rhythm, which are temporary and without unfavorable prognostic significance. In some individuals tea, coffee, and tobacco immediately produce arrhythmia of the pulse. Mackenzie imputes a very grave prognostic significance to the appearance of an irregular pulse during a fever in patients who otherwise have normal pulses, and states that a fatal outcome occurred in all his cases of croupous pneumonia which had an irregular pulse before the crisis, even though the irregularity was only occasional. It is certainly true, particularly in pneumonia, that the appearance of irregularity in the pulse is of very grave import, but the author does not care to subscribe absolutely to such a pessimistic belief in reference to arrhythmia in fever (such arrhythmia in pneumonia also is due to extrasystoles), because he knows patients who immediately develop arrhythmia with innocent febrile disturbances. Upon the other hand, a habitually arrhythmic pulse very frequently tends to become regular during fever.

We may differentiate between an *absolutely irregular pulse* (pulsus irregularis), which is usually at the same time much increased in rate (delirium cordis), and *a partially irregular pulse*. In one type of the latter the irregularities are uneven, *i. e.*, the intervals between the beats are sometimes shortened and sometimes lengthened without any sign of regularity. In the other type of the *partially irregular pulse* the irregularities are periodic, *i. e.*, they follow each other at regular and definite intervals.

Irregularities of rhythm are nearly always associated with inequality of the individual pulse-wave, *i. e.*, a pulsus irregularis is at the same time a pulsus inequalis. It is therefore advisable to defer the consideration of the various types of irregular pulse until after we have studied and understood the difference in quality of the individual beat. (See Sphygmography.)

CHARACTERS OF THE INDIVIDUAL PULSE-BEAT

The proficiency which different observers attain in the determination of the quality of the individual beat by palpation varies decidedly with their practice and skill. He who is less adept may obtain more accurate

information by employing sphygmography, sphygmomanometry, and sphygmobolometry. In addition to the regularity, the qualities which every physician should recognize by palpation without any especial instrument are: the celerity, the tension, the size and strength, and dicrotism.

Celerity of the Pulse.—By celerity is meant the degree of rapidity of the rise and subsidence of the individual pulse-wave beneath the compressing finger or, if the pressure be graphically recorded in the sphygmogram, by the steepness of the rise and fall of the curve. To recognize the degree of celerity by palpation three fingers should be employed, placing them along the course of the artery.

A *pulsus celer* is one whose wave rises quickly and descends quickly; a *pulsus tardus,* one whose wave rises slowly and descends slowly. Upon the fingers a *pulsus celer* produces the impression of a quick, sharp rap. This peculiarity is appreciated most distinctly when the pulse-wave is at the same time of considerable volume. Therefore, what is often called a pulsus celer is generally a full pulse as well. The pulse of aortic insufficiency is the most striking as well as the commonest example of a pulsus celer. It very frequently can be appreciated even by the eye as a noteworthy pulsation of the artery in the neck, and the diagnosis of aortic insufficiency made correctly at a distance. The abruptness of the ascent and of the descent of the pulse-wave do not take an equal part in producing this "rapping" sensation. For although the abruptness of the rise may be recognized without any particular training, it requires considerable practice to recognize the abruptness of the drop. Von Frey claims that the abruptness of the descent of the pulse-wave can be estimated only by means of the sphygmograph and not by palpation. But the author believes that an expert physician can perfectly well differentiate between a pulse whose sharp, bounding quality is due only to an abrupt onset of the wave and a pulse with an abrupt descent as well as ascent. The terms "pulsus celer" and "pulsus tardus" are especially well adapted to the cases in which both limbs of the pulse-wave are either steep or blunt. Where either the ascent or the descent alone is abrupt or gradual, this peculiarity should be specified. Thus, a pulse may be *celer* in its ascent and *tardus* in its descent. These conditions are explained more fully by Sphygmography upon p. 143 (Figs. 65–69).

Pulse Tension.—Consideration of Blood-pressure.—We consider under the term "pulse tension" the qualities of the individual pulse-wave which show the amount of pressure in the arteries. The difficulty is, however, that the term blood-pressure may be understood in quite different ways. The term blood-pressure ordinarily signifies the average or mean blood-pressure which physiologists have almost exclusively studied with the usual manometers in experiments upon animals. But the maximum or systolic and the minimum or diastolic blood-pressure must also be considered. In a healthy man or animal the variations of blood-pressure from the average are but of moderate degree, and so we ordinarily speak of "blood-pressure" without further remark when we strictly mean average blood-pressure. We do not know, however, whether the systolic variations in pressure under pathologic conditions are so very slight. Sphygmographic and sphygmomanometric observations (see later) seem to show that they are considerable. Therefore, under pathologic conditions, the systolic

or maximum, the average or mean, and finally the diastolic or minimum, pressure should be considered separately. (See Absolute Sphygmogram, p. 174 et seq.) A more distinct and uniform conception of the terms expressing the pulse tension is, therefore, essential, and these terms should be clinically correlative to blood-pressure. Just as we distinguish between a maximum, middle, and minimum blood-pressure, so should we differentiate between a maximum or systolic, an average or mean, and a minimum or diastolic tension of the arteries. The ordinary definition that tension is the measure of the amount of finger pressure which is necessary to compress the artery is not accurate, and is, therefore, inadequate to teach us how to palpate pulses correctly. It is better to define the maximum tension of an artery as the amount of force which is necessary to prevent the transmission of the pulse-wave to the periphery,[1] the minimum tension as the power necessary to compress an artery during cardiac diastole, and the average or mean tension as a certain average amount of power which will suffice to close the artery between systole and diastole. A disregard of the various meanings of the term arterial tension thus explains the variations in the description of one and the same pulse, one observer calling the tension high, another calling it low.

As the manner of palpating an artery varies, so do conclusions as to the pressure conditions in the artery differ. Usually—although only partly justifiably—most importance is attached to the maximum or systolic tension of the artery. This is determined ("dynamic" procedure of taking the pulse) by palpating the artery with three adjoining fingers along the long axis of the vessel. The distal finger compresses the artery so that no recurrent pulse-wave can reach the vessel from the periphery. The proximal finger exerts a gradually increasing pressure upon the artery until the middle finger, which should rest quite gently upon the vessel, can no longer feel the wave. The power used is the measure of the (heart) systolic or maximum tension of the artery. This procedure is imitated by von Basch's method of sphygmography (p. 163 et seq.).

The physical accuracy of his method of determining the systolic pressure, *i. e.*, the correctness of identifying the amount of pressure employed with the systolic pressure, is questionable. The same doubt applies to this dynamic method of palpation, for the reason that, besides the systolic increase of pressure, the vital energy of the pulse-wave has an important influence upon the result obtained. This vital energy is closely dependent upon the *size* of the pulse-wave, and the size in turn by no means runs parallel with the blood-pressure. We have not only the systolic blood-pressure to overcome in the procedure, but, generally speaking, a much greater pressure, because the recoil of the pulse-wave at the compressed point of the artery acts very much as a water-ram.

It will, however, be shown in the chapter upon Sphygmomanometry that this theoretic objection plays no important rôle in the practical results obtained by dynamic palpation. The conditions are identical with those in von Basch's and Riva Rocci's method of sphygmomanometry, in which, as shown at p. 166, the vital energy or the size of the pulse-wave does not markedly influence the value of the systolic pressure found. A greater objection to the determination of systolic pressure by palpation appears to be the fact that the force necessary to compress an elastic tube filled with fluid is dependent, not only upon the pressure within, but also upon the caliber of the tube. From Pascal's law of the hydraulic press it follows that every unit of surface of the vascular wall is subjected to the same pressure, so that when an attempt is made to compress an elastic vessel, the size of the area com-

[1] See the following pages for the doubts about identifying this exercise of power with the systolic pressure.

pressed must also be regarded, as well as the manometric pressure. Consequently, with the same manometric pressure a large vessel is just as many times as difficult to compress as a small vessel, as the surface of the former is greater than that of the latter. In sphygmomanometry this objection is happily overcome by the employment of a pneumatic compressor; in dynamic palpation, however, the objection seems to be a practical one. Experience, nevertheless, teaches that with training this objection can be overcome sufficiently in a great majority of cases, even in palpation, to estimate, at least approximately, the systolic tension as high, medium, or low. According to the author's view, this rather unexpected applicability of palpation is due to the fact that the palpating volar surface of the terminal phalanx bears a certain physical resemblance to a fluid "pelotte," and that the bony phalanx does not compress the artery directly, but indirectly through the medium of the hydraulic cushion of the finger-pulp. The conditions present are, therefore, quite similar to those in von Basch's sphygmomanometer. This completeness of the sense of touch is a new example of the teleologic adaptation of the human body, not only to the palpation of the pulse, but to similar palpatory tasks which were practised by aboriginal man (the determination of the ripeness of berries, etc.).

A beginner may facilitate his task by palpating the vessel through an interposed pneumatic cushion, as, for example, the pelotte belonging to the author's sphygmomanometer. (See p. 165 et seq.) The tube is clamped, and instead of being connected with the manometer, the pelotte is moderately distended, and placed between the artery and the palpating finger. When employed in this manner, it constitutes the simplest form of a palpatory manometer.

The author's so-called "static" method of palpating the pulse is as follows: If the radial artery be palpated with one, two, or three fingers, we observe that with a very slight pressure the appreciable pulsatory excursions of the artery are usually very small, but that they increase as soon as the arterial wall is somewhat more strongly compressed. With increasing pressure a maximum excursion is observed, after which any further increase of digital pressure diminishes the size of the pulse. The amount of pressure necessary to obtain the maximum excursion corresponds to a certain mean between the minimal, *i. e.*, the diastolic, and the systolic pressure in the artery, as is shown by the results obtained by sphygmobolometry. (See p. 180 et seq.) The increased excursion of the artery with increasing external pressure is evidently due to the fact that in the uncompressed artery a part of the pulsatory increase in pressure is absorbed by the tense arterial wall; when this tension of the arterial wall is relieved by pressure from without, the pulse-wave will be transmitted to the palpating finger with a minimum amount of loss and further increased by reflexion, so that the excursion of the palpating finger is considerably increased by both factors. While in the former edition the author held the opinion that the pressure exerted by the finger at the moment of maximum excursion corresponded to the minimum pressure in the artery, the comparative examination of the pulse by means of sphygmobolometry (see p. 180 et seq.), and the manometric determination of minimum pressure (see p. 175 et seq.), teach that the maximum excursions correspond to a certain mean pressure, in which the reflux and the relief of tension of the arterial wall are combined to the best advantage. It might, therefore, be said that this static procedure for determining blood-pressure by palpation gives information in reference to a mean arterial pressure, but it should particularly be remembered that this mean pressure is by no means the exact arithmetic mean between the maximum and the minimum pressure. When the finger pressure is increased until the palpating finger attains the maximum excursion, any further compression will, of course, diminish the excursion, since the pulse-wave is no longer able to overcome the resistance of the compressing finger. In this method the ability of estimating the pressure employed also depends upon the previously mentioned hydraulic peculiarity of the digital pulp.

In considering these theoretic difficulties, we can readily appreciate the fact that an especial skill in appreciating the relations of pressure accrues to the careful clinician only after years of practice and a long experience in contrasting and remembering differences in pressure. On account of such manifold difficulties in judging arterial tension it is advisable to supplement palpation by sphygmomanometry (p. 163 et seq.).

Custom has come to employ the expression "hard" or "tense" pulse (pulsus durus) as synonymous with increased arterial tension,

and "soft" or "relaxed" pulse (pulsus mollis) with diminished tension. Of course, we must not confuse these with the same terms applied to qualities of the arterial wall (softness *versus* rigidity of the artery) (p. 108). Again, these terms may at one time be applied to the systolic, at another to the diastolic, pressure. In nephritis and arteriosclerosis the diastolic as well as the systolic pressure is ordinarily increased.

In the latter, however, the pressure may be normal, particularly when the splanchnic area is not involved in the arteriosclerotic process. This peculiarity should never be employed to favor the diagnosis of arteriosclerosis. (See p. 109.) In reference to the diagnostic utilization of blood-pressures obtained by palpation, the reader is referred to the chapter upon Sphygmomanometry. (See p. 163 et seq.)

THE ESTIMATION OF THE SIZE AND ENERGY OF THE PULSE
(The Strength, Power, or Volume of the Pulse)

When we determine the maximum excursion of the pulse beneath the appropriate pressure of the palpating finger in the "static" method, as just described, we determine that factor which is designated in the sphygmogram as the size or height of the pulse. Although this value is derived from the difference between the maximum and minimum arterial pressures, and consequently is proportional to the height of the absolute sphygmogram (the difference of the heights of the points in Fig. 101, p. 177), it has, nevertheless, an indefinite significance in reference to the estimation of the amount of work done by the heart, since the lifting power of the pulse-wave is dependent not only upon these differences of pressure, but also upon the diameter of the artery (Pascal's Law, see p. 141). In other words, with the same difference between maximum and minimum pressure the palpating finger will be elevated more with a large artery than with a small one. In estimating the work done by the heart, the size of the pulse consequently affords even less accurate conclusions than does the absolute sphygmogram (see p. 177), because the calculation includes an additional unknown factor, namely, the diameter of the artery.

When we come to consider the strength of the pulse, however, we find quite a different state of affairs. This idea of pulse energy, which the older physicians considered second in importance only to the hardness or tension, has been recently neglected, evidently as the result of the introduction of the exact methods of measuring blood-pressure. The entire attention of the practitioner has been directed to the statics of the arteries, and some who believe that the determination of arterial pressure is all sufficient even regard the determination of the strength of the pulse as less exact and less scientific, since it comes to us from a period when the palpation of the pulse was most rudimentary. Such a conception, however, is entirely erroneous, and it is urgently necessary to introduce again this idea of pulse strength or pulse energy in our clinical teaching, because it has been sufficiently shown by the author's investigations in reference to the absolute sphygmogram that the height of the curve or of the pulse-pressure (the arterial maximum and minimum pressure) is of but little value in estimating the amount of work done by the heart. This is due simply to the fact that static conceptions can never be made the measure of a movement as long as the resistance to that movement is unknown. The term strength or energy of the pulse,

upon the other hand, is a dynamic conception, and it is clear that it can give us information up to a certain point as to work done by the heart. For the facts upon which this statement is based the reader is referred to the section upon Sphygmobolometry. (See p. 180 et seq.) As the work done by the heart may be measured by the sphygmobolometer, so can the energy of the pulse be estimated by the sensation transmitted to the palpating finger. It is not the blood-pressure nor the height nor size of the pulse-wave, but the actual energy of the pulse-stroke, which is determined. Our organism is much better adapted to such an estimation of mechanical energy than it is to the estimation of arterial pressure, because in the latter Pascal's law is always responsible for certain difficulties, and while these may be overcome to a certain extent by practice, the law plays no part whatever in the determination of pulse energy. Although the pulse-beat in a larger artery develops a greater amount of energy according to Pascal's law, this is simply an expression of the fact that in this case the pulse energy is greater as a result of the larger volume of blood set in motion. The fundamental difference between this method of examination and the determination of the height or size of the pulse-wave becomes clearest when we remember that the height of the pulse-wave is a linear measurement, while the strength of the pulse is a complicated one, represented by the formula $\frac{M.v^2}{2}$, in which v is the velocity of the ascending limb of the curve and M the mass of blood acting upon the finger during a pulse-beat. It, therefore, seems important to rehabilitate this primitive conception, which is the most correct and clear of all theoretic considerations in reference to the pulse.

As to how far we may go in deducing conclusions from the radial pulse in reference to the total work done by the heart, we would refer the reader to the chapter upon Sphygmobolometry. From the explanations which will be made of the technic of sphygmobolometry it also follows that palpation gives the most correct estimation of pulse energy when the artery is completely closed peripherally by one finger of the left hand, and pressure is made proximally by the palpating finger, as in the previously described static method (see p. 117), until the maximum pulse is obtained. Under these conditions the strength of the pulse-beat represents the energy of the pulse. The author would differentiate this from the previous methods of palpating the pulse by designating it as *the energetic method.*

Dicrotic Pulse.—We speak of a pulse as being dicrotic when a second wave follows immediately after the principal rise. (The nature of this will be discussed under Sphygmography, p. 130 et seq., and p. 146 et seq.) A dicrotic pulse furnishes a certain sense of after-beating to the palpating finger. It is usually associated with diminution of the minimum pressure. Both the primary and the secondary wave are felt to be greatest when the palpating finger presses only lightly; therefore a dicrotic pulse is best appreciated with gentle pressure. This can be readily understood from the explanation given of the excursion of the arteries (p. 117 et seq.). The beginner is apt to employ too great pressure to recognize such a condition readily.

It should also be noted that, upon the one hand, dicrotism may be simulated by early extrasystoles, while, upon the other, it may simulate

a pulsus bigeminus or a pulsus alternans. (See Fig. 63, p. 142.) This error may be prevented by simultaneous auscultation of the heart, which will determine the number of cardiac systoles.

Combined Qualities of the Individual Pulse.—We have a number of terms which refer to a pulse which comprises two or more of the qualities already described. Of these, we shall mention only those in most common use: pulsus fortis, strong pulse = large + tense (corresponding in quality to a pulse of great energy, see p. 118); pulsus plenus, full pulse = large and medium hard; pulsus debilis s. inanis, weak or feeble pulse = small + weak; pulsus undosus = large + soft; pulsus serratus = large + tense + rapid; pulsus vibrans = very large + very tense. This name is applied because the so-called elasticity elevations (see p. 130) may be distinctly appreciated by palpation. These terms are fitting enough, but rather unnecessary. Instead of employing them, it is better for a beginner to mention the individual qualities one after another. The Latin terms are sometimes combined. For instance, we speak of a pulsus tardodicrotus or a pulsus magnodurus, etc. Such combination terms are practical enough in themselves, but some of them are not sufficiently clear, considering the double meaning of the terms "celerity" and "tension" (see above). In general a detailed description is better than an attempt to describe the pulse by one word.

Further consideration of the significance of the qualities of the pulse will be taken up in conjunction with sphygmography, because some details may be certainly obtained and explained only by means of this method. This is particularly true of certain complicated peculiarities having most to do with changes in the pulse rhythm.

SPHYGMOGRAPHY

Sphygmography is the method of registering the pulse-wave of some peripheral vessel, generally the radial artery, upon a moving surface (usually smoked paper), by means of a special instrument, the sphygmograph.

INSTRUMENTS

Vierordt constructed the first sphygmograph, and since then a great many improved instruments have appeared. Most of them, however, have retained Vierordt's principle of transmission by means of a lever. The best known and most frequently employed sphygmographs are: Marey's, for a long time the only one used clinically; Landois', Sommerbrodt's, Riegel's, Dudgeon's, Jaquet's, and v. Frey's. Dudgeon's apparatus has been a favorite, because with it curves of considerable excursion are easily traced. Recently it has been discredited on account of the marked tendency to extensive swinging of the registering lever; but if we are not concerned with the form of the individual pulse-waves, it may be employed in the analysis of pulse-arrhythmia. (See p. 155.) Mackenzie has also adopted it for his polygraph (Fig. 52, p. 129). It possesses the same advantage as Jaquet's sphygmograph in that extended series of pulses may be recorded upon long strips of paper; but the latter is an improvement and includes a really excellent mechanism for marking intervals of time.

v. Frey's sphygmograph,[1] also a very excellent instrument, is depicted in Fig. 44. It possesses this advantage over other instruments: the motions of the pulse are transmitted to the writing-lever as simply as possible. The method of employing this instrument is as follows: The most superficial part of the radial artery is marked upon the wrist with a skin-pencil; and the apparatus is adjusted so that the "pelotte" impinges exactly over the indicated artery, and with the drum toward the elbow. It is then fastened to the forearm by means of the carrier or slide, *S*, with a strap.

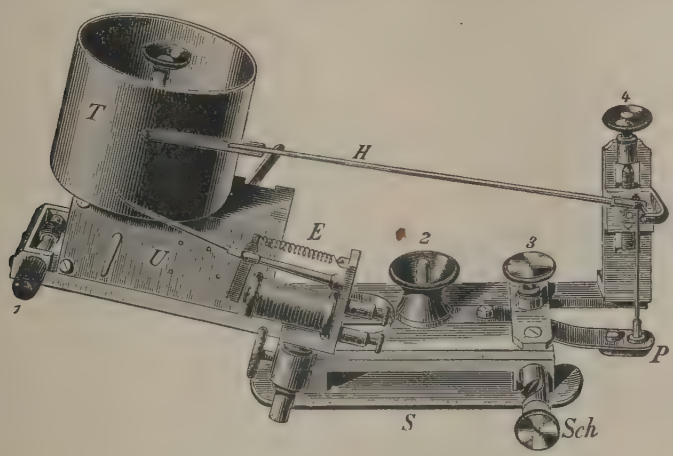


Fig. 44.—v. Frey's sphygmograph.

The carrier (Fig. 45) is fastened separately with the hooks that are attached for this purpose. The screw *Sch* serves to fix the strap. Loosening screw 2 makes it possible to move the entire apparatus upon the "carrier." This is very convenient for the purpose of adjusting the "pelotte" more accurately. By means of screw 3 we attempt to regulate the amount of pressure upon the pad until the lever needle begins to make excursions. The apparatus is then firmly fixed in place by tightening screw 2.

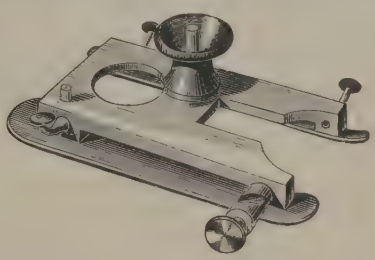


Fig. 45.—The carrier or slide of v. Frey's sphygmograph.

The drum has, of course, been removed from the apparatus before this, covered with wax paper, smoked[2] by revolving over a flame, and then replaced upon the clock mechanism, *U*. By turning key 1 the drum can be moved so that the bent

[1] v. Frey, Die Untersuchung des Pulses, Berlin, 1892, J. Springer.

[2] A pointed gas-flame is perhaps the best source for smoking, or a kerosene lamp without a chimney, or a piece of burning camphor. We must be careful not to smoke too thickly, because the friction between the registering needle and the drum would then be so great that the curve would be disturbed.

point of the registering needle rests lightly upon the smoked paper. The height of its excursion and, hence, of the curve can be regulated by turning screw 3, which controls the tension of the "pelotte." The clockwork is then started by means of the lever which is visible behind the writing-lever *H*, to the right of the drum. The drum revolves, and the bent point of the needle registers the sphygmographic curve upon the smoked drum. The drum is then taken off again, the paper carefully cut off, separated from the drum, and fixed in a 5 to 10 per cent. alcoholic solution of shellac or in a 10 per cent. solution of dammar balsam in benzin. The part *E*, which has not yet been described, is a small electromagnet with a registering needle attached to the armature, so that it registers upon the drum. When connected with an electric current, intervals of time or signals may be indicated in the same way as is customary in physiologic experiments. When not being used, it may be disconnected.

Von Frey has since modified his sphygmograph—and, it would seem, very advantageously. The chief improvement is the substitution of a delicate metal spring for the joint connections, so that the motions of the registering needle are less angular. Besides this, the drum is connected with a Jaquet's chronometer works, so that the time intervals are pictured. The curve may, of course, be registered by means of air transmissions upon a kymographion placed at some distance.

Jaquet's sphygmograph[1] (Fig. 46) consists of a metal frame, *D—p*, to which is sewed a cuff, *B*, *B*, for attaching to the wrist. The sphygmograph proper, *A—r*, is attached to the frame. The window cut out of the frame is to be applied accurately along the radial artery (previously marked out with a pencil), and the cuff then strapped around the wrist quite tightly. The sphygmograph proper is set into the frame by hooking into the hinge, *p;* and then the connection of the two parts is effected by pressing down at *r* and tightening the screw *m*. The pulse-registering apparatus consists of a short, broad spring, which presses upon the artery and transmits its movements to the registering needle by means of the lever system *d e f*. The screw *m* also serves to adjust the registering needle at the desired height upon the smoked strip of paper. By screwing it down, the spring *d* is pressed against the artery. The screw *c* is connected with an "eccentric" contrived to increase or diminish the pressure upon the spring. The amount of pressure can be determined by noting the position of the figures upon the screw. For the rules in reference to the amount of pressure or to the desired height of the curves see p. 140 et seq. With this mechanism the instrument can be adjusted with practically equal pressure in each case, and taken away from the frame and reapplied in the same case without alteration of the pressure. Jaquet's instrument, like Dudgeon's, writes upon a flat and not, as most other sphygmographs do, upon a curved surface. Another advantage consists in the very slight and constant amount of friction between the writing-needle and the paper, so that there is very little trouble in adjusting the registering part of the apparatus. The paper lies horizontally; it need not be especially strong, and it may easily be 40 or 50 cm. long. The little box *a* contains the clockwork which moves the strip of paper, *p*. This is started by pressing down on lever *b*. The rate at which the paper moves may be increased from 1 to 4 cm. per second by altering the position of lever *a*. The slower motion produces a curve which presents a better general idea; the more rapid motion, one which may be more accurately analyzed. This rate of motion may be altered while the sphygmograph is in action. The box *a* also contains a stop-watch device connected with the time-registering mechanism, *S*. The latter consists of a small pen which registers a mark upon the margin of the smoked ribbon every fifth of a second (Fig. 54).

The old style of the Jaquet sphygmograph, illustrated in Fig. 46, has the disadvantage that the individual parts of the pulse-registering mechanism are not connected firmly enough to insure their constant contact with every change in the rate of motion. At *e* and *d* the movements of the lever system are transmitted by loose joints. This is not a disadvantage when the excursions are slow, since the parts are held in contact by the metallic ball which is visible at the top of the apparatus. When the excursions are rapid (increased frequency of the pulse, great elevation of the pulse), however, the oscillations of this mechanism may give rise to errors. These consist particularly of the appearance of artificial elevations in the pulse curve, dependent entirely upon the apparatus. One part of the lever system may advance independently until it meets with resistance; then, at the moment of the occurrence

[1] Described in Zeit. f. Biol., vol. xxviii, N. F., x. Manufactured by Schüle, at that time Mechanic to Physiologic Institute of Basel, now Director of the Institute for Scientific Chronometry, previously at St. Imier, Canton Bern, but since April 1, 1907, at St. Johannring, 26, Basel, Switzerland.

of this resistance, there is a jolt of the writing-lever, which appears as an artificial elevation in the curve, corresponding to nothing whatever in the pulse-wave. In addition to the occurrence of these artificial elevations, the oscillation dependent upon the defective connections of the parts of the lever system also causes an increase in the height of the curve. As we shall subsequently learn (p. 141), it is difficult under any circumstances to gain an idea of the volume of the pulse from the height of the curve, and this error of oscillation renders the employment of the sphygmograph for this purpose still more questionable. A further source of error is the fact that the rate of motion of the needle at the moment when the individual parts of the lever system are not in contact is dependent upon the weight of the small metallic

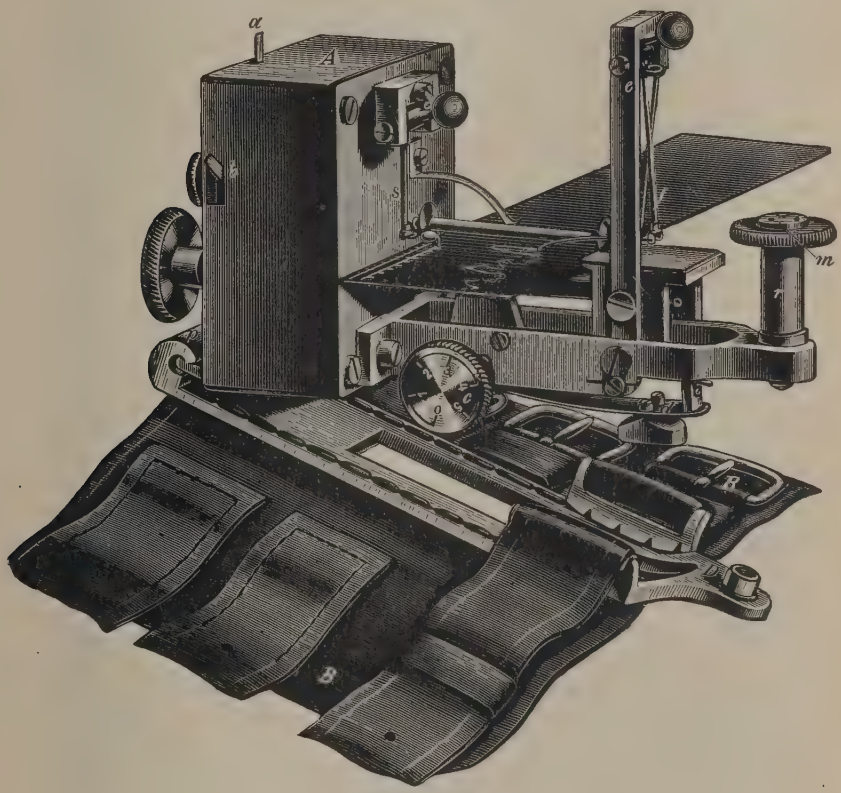


Fig. 46.—Jaquet's sphygmochronograph (old style).

ball. Jaquet himself has criticized these faults of his apparatus, which he copied from the Dudgeon sphygmograph, and has recently attempted to overcome them by a rearrangement of the recording mechanism, of which he gives the following description,[1] and the accompanying diagrammatic drawing (Fig. 47): "The movements of the pelotte (spring *a*) are transmitted to the bent lever *c c* by means of a wedge-shaped blade, *b*. The upper extremity of the bent lever is marked at *s* by a carefully made screw-thread which works in a corresponding cog-wheel, bearing the writing-lever. The contact between the screw-thread and the cog-wheel is insured by a spring, *e*, which constantly presses the lever *c c* against the cog-wheel. In addition to this the bent lever *c c* does not turn upon an axis passing through its

[1] Münch. med. Woch., 1902, No. 2.

angle, as in the old instrument, but about the point *f*, and the axis of rotation is replaced by a short, flat watch-spring which insures the contact between the lever *c* and the edge *b*. This spring is so short that individual oscillations are not to be feared, since the length of such an oscillation is less than $\frac{1}{500}$ of a second, and is consequently trivial in comparison to the velocity of the pulse-registering mechanism. This spring also renders unnecessary the eccentric of the old instrument, since its tension is sufficient to overcome the resistance which the stretched skin offers to contact with the pulsating artery. The ratio of transmission in the short arm of the lever *c c* is 1: 2, and that between the cog-wheel and the writing-lever 1: 50, so that the total enlargement amounts to 1: 100."

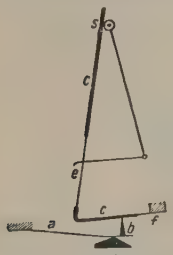


Fig. 47.—Diagram to explain the improved mechanism in the registering lever of Jaquet's sphygmochronograph.

An artificial pulse has been constructed by Langendorff, upon a principle first employed by Donders, in which a revolving eccentric transmits to the pin of the sphygmograph excursions similar to those of an arterial pulse. Jaquet, by the use of this mechanism, found that his modified sphygmograph records the movements of the pulse accurately and without oscillation for all of the velocities usually encountered in sphygmography.

In spite of the marked improvements obtained by these changes, it seemed to the author that the construction of the modified Jaquet sphygmograph was still open to some objections, and particularly because there was not a firm connection between the blade *b* and the lever arm *c* (Fig. 47); if the velocity was very great or the pulse-rate very rapid, the parts *c* and *b* became separated, and thus still produced artificial elevations in the curve. The oscillating pad was a further disadvantage of the old instrument which had not been overcome in the new modification. In both the old and the improved models this pad was connected to the spring *a b* by a loose joint. This naturally simplified the application of the spring to the artery, but from the lack of a firm connection it also produced distortions of the curve. In order to obviate these faults Schüle, who made the improvements in Jaquet's modified sphygmograph, has, at the author's suggestion, attached the pad firmly to the spring, as in Marey's and v. Frey's sphygmographs, and also connected the arm *f c* of the bent lever with the blade *b* by a small wire stirrup, which passes over the lever from the edge of the blade, so that any separation of the blade and the lever is rendered impossible. This mechanism, recommended to the author by Schüle, acts like a hinge joint, but possesses none of its disadvantages. By these modifications the entire lever system has been united into a firm whole, in which no displacement is possible without implicating the entire system, and which must consequently accurately represent the movements of the arterial wall, disregarding the possibility of the oscillation of the entire system, a condition that the author has been able to exclude, for the velocities ordinarily encountered in sphygmography, by tests with Donders' artificial pulse. The jointed connection of the edge with the bent lever has the additional advantage that we may employ the eccentric of the original apparatus, which the author sorely missed in the improved Jaquet sphygmograph, since it not only greatly facilitated the application of the sphygmograph and rendered possible the necessary variations in the tension of the spring, but also permitted us to obtain in every pulse-tracing exactly the same amount of tension of the spring with the same position of the pencil. The writer believes that Jaquet's sphygmograph, with these different improvements, now answers all reasonable requirements. It, of course, produces lower curves than the old model, on account of the suppression of oscillation. The Institute for Scientific Chronometry, James Jaquet, A. G., previously in St. Imier, now in Basel, adds the described improvements to the old Jaquet sphygmograph for 28 to 35 francs, according to the condition of the instrument, and also furnishes the modified sphygmograph at the original price of 165 francs. This firm has constructed an additional model (Model I), which differs from the original in that all the lever connections are hinge joints and consequently less sensitive to misuse. Model I is now supplied unless a special request is made for Model II, which possesses the author's modifications above described.

Even those observers who recognize that low pulse-curves are truer to nature may sometimes wish to produce a curve of larger excursions, particularly when the pulse is small and weak, or when information is desired in reference to rhythm rather than to the form of the curve. This firm has consequently constructed for the author a third model, in which the excursions of the curve may be varied at pleasure. On account of technical difficulties this is effected, not by changes in the lever enlarge-

ment, but by a modification of the strength of the spring in the pelotte. With a pulse of constant energy, the stronger the spring, the less will be the excursion of the writing-lever, so that by changing the strength of this spring we may modify the height of the curve precisely as if we changed the length of the arm of the lever. As a matter of fact, this principle is employed up to a certain point in the accurate application of the ordinary Jaquet's sphygmograph. In this third model, the original tension of the spring is different, and by means of an eccentric the tension may be varied to suit any individual case. This change in tension is brought about by a sliding mechanism which moves downward toward the free end of the spring and thus shortens its working length. The author is convinced that by means of this mechanism the height of the curve may be varied throughout a most extensive scale. In order that the purpose of this mechanism be not misunderstood, it should be noted that the tension of the spring is not supposed to be varied with each record, since this is superfluous and unnecessarily complicates the technic. The mechanism simply makes it possible for those who desire high curves to set their sphygmographs permanently with a "long spring," while those who prefer a reduced height of the curve, and the lessened tendency to jolting, may work with a "short" or "medium" length spring. In fact, the mechanism should always be employed with a constant tension

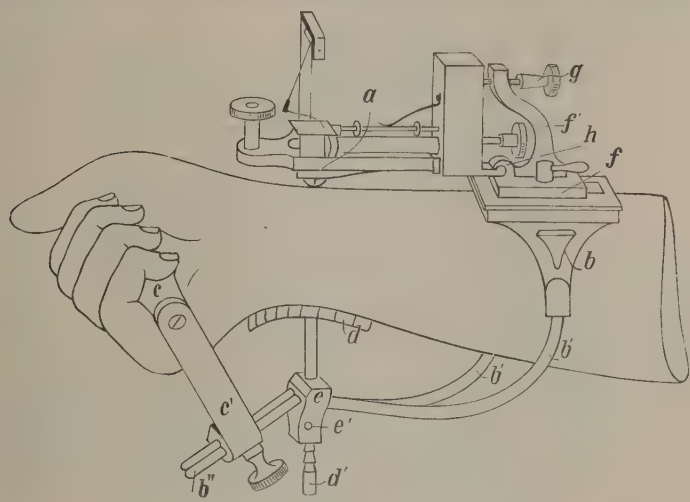


Fig. 48.—Appliance for fixation of Jaquet's sphygmograph.

when it is desired to compare the records of different curves, particularly in reference to the maximum height obtained, since, if the tension of the spring be varied as well as the eccentric and the setting-screw, the conditions become so complicated that the possibility of comparison is lost. This fact naturally does not forbid utilizing a change of tension of the spring as a third aid in obtaining a record in a particularly difficult case. This form of the sphygmograph is supplied by the manufactory as Jaquet's Sphygmograph, Model No. III, with variable spring tension.

At the author's suggestion, the manufacturers attach the base of the new Jaquet's sphygmograph to a movable padded metal frame, in order to avoid compressing the artery by the ground-plate of the sphygmograph when the mechanism is firmly applied. This metal strap forces the artery upward to a certain extent and bridges it over above the pelotte.

F. Runne's laboratory in Heidelberg, for the manufacture of instruments of precision, has recently constructed a very practical appliance for the fixation of Jaquet's sphygmograph by means of which the instrument may be applied without any circular constriction whatever. Fig. 48 clearly shows its application, and requires no description except that the screw *g* replaces the setting screw of the original sphygmograph, since it presses the pelotte upon the artery by leverage.

The Employment of Jaquet's Sphygmograph as a Small Clinical Kymograph.—If it be desired to make graphic records of any kind (from a pen attached to a float,

for example) upon a vertical writing surface, any of the kymographic appliances may be employed. If such a mechanism cannot be obtained, the appliance illustrated in Fig. 49 may be utilized. It was constructed for the author by the manufacturers of the Jaquet sphygmograph. It consists of a long plate, which is provided with a double row of small rollers, as shown in the illustration, which guarantee an accurate movement of the paper strip of the sphygmograph, even in the vertical position. The sphygmograph itself is attached in the middle of this plate (Fig. 49), and serves simply as a motor for the strip of paper, while the writing appliance employed may vary (Marey's air cushion, a pen attached to a float, etc.). The time registering mechanism of the sphygmograph may also be employed in this position. In such experiments the strip of paper is quite narrow, and to adjust it to the proper height

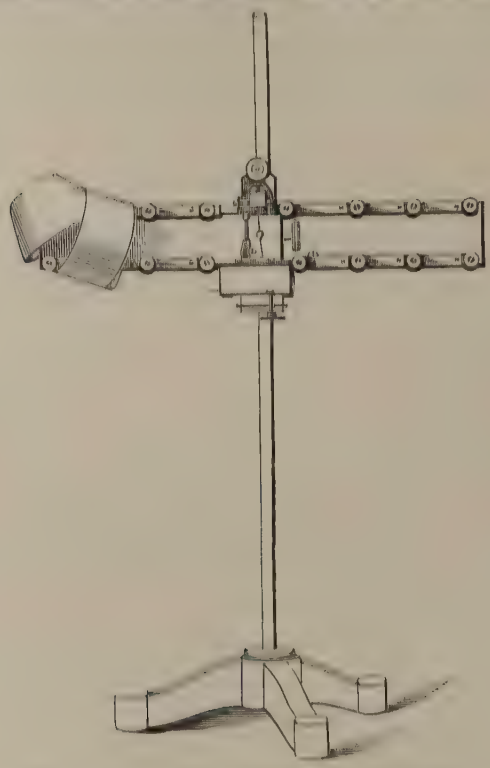


Fig. 49.—Jaquet's sphygmograph used as a kymograph.

the sphygmograph and its plate are fastened to a vertical rod by a sliding attachment. This appliance was used by the author for his sphygmobolometric records before he constructed the simple writing mechanism of the present sphygmobolometer. The curves depicted in Fig. 7 in his original work upon sphygmobolometry (p. 175) were recorded in this manner.

INSTRUMENTS FOR THE SIMULTANEOUS REGISTRATION OF THE ARTERIAL PULSE AND OF OTHER PHENOMENA OF MOTION

JAQUET'S CARDIOSPHYGMOGRAPH (Fig. 50)

We are indebted to Jaquet for the construction of an instrument designated as the cardiosphygmograph, which makes it possible to obtain upon a single broad

strip of smoked paper the radial pulse, together with two other phenomena of movement, such as the apex-beat, the carotid pulse, the venous pulse, the liver pulsations, or the respiratory excursions. This instrument is depicted in Fig. 50.[1] The three curves are recorded in a parallel manner, as shown in the illustration. For additional clearness the curves are depicted in black upon a white background in the figure, while the opposite condition obtains in the actual mechanism. The instrument, as a whole, corresponds in its construction to that of Jaquet's sphygmograph (Fig. 46, p. 123), but with the difference that two pneumatic registering appliances, *E E*, are added to the direct recording mechanism for the radial pulse. It is consequently larger, but nevertheless easily transportable. Like Jaquet's sphygmograph, the cardiosphygmograph is also provided with excellent clockworks, *A*, which mark fifths of a second upon the strip of paper by means of the writing mechanism *a*. This apparatus is also supplied with the metal frame recommended by the author (p. 125), which protects the radial artery from the pressure of the base of the instrument when it is buckled about the wrist. In the newer instruments the loose connections between the sphygmograph spring and the writing-lever are replaced by firm ones, in accordance with the principles stated upon p. 124 et seq., and the

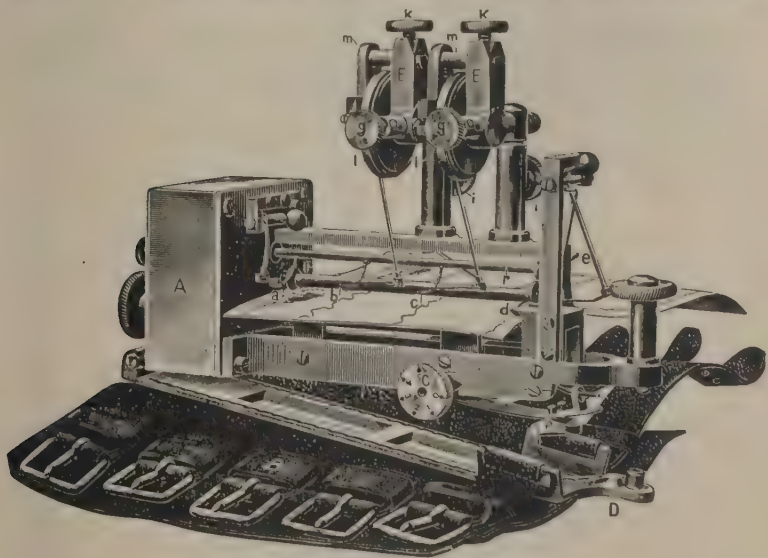


Fig. 50.—Jaquet's cardiosphygmograph.

small spherical ball depicted above *c* in the illustration is consequently omitted. The connections are made by hinge-joints, as in Jaquet's sphygmograph, Model I (p. 124), and there is also a similar connection between the air-cushion (pelotte) and the writing-lever. The arresting mechanism, *b, c, d*, is attached to an axis which may be rotated by the lever *e*, thus raising the three writing points while the strip of paper is introduced. Upon the posterior surface of the apparatus, partly visible in the figure, are found the openings by means of which the writing drums *E E* are connected by tubes with the pneumatic recording appliances. The remaining parts of the apparatus will be sufficiently understood from the figure and from the description of the sphygmograph on p. 122 et seq. The rubber membranes of the writing-cushions may be easily replaced when damaged; the best material for this purpose is the rubber membrane employed in the preparation of the desmoid capsules. (See Examination of the Stomach.) In the directions for use accompanying the instrument are found the necessary instructions for the manipulations required in changing the membranes. In most cases, particularly for the carotid

[1] This instrument may be obtained from the firm of James Jaquet, Institute for Scientific Chronometry, A. G., Basel, St. Johannring, 26.

pulse, the venous pulse, the hepatic pulsations, and even for the apex-beat (see Cardiogram) and the respiration (see p. 100 et seq.), small glass funnels may be employed as pneumatic receivers. The size of the funnels must be varied with the individual case, but generally it is well to employ the smallest funnel possible. These funnels are attached to the free ends of the tubes connected with the writing drums, and they are then held in air-tight connection with the part of the body selected while the curves are being recorded. The length of the tubes is immaterial, since the pulsating variations in pressure are transmitted through air with the same velocity as sound. For recording the apex-beat Jaquet has constructed a special receiving appliance, which is described and illustrated in the section upon Cardiography.

At the author's request Jaquet's sphygmocardiograph has recently been combined with an appliance for the graphic marking of the cardiac sounds, and this instrument is supplied by the manufacturers in reduced form as the "Simplified Jaquet's Sphygmograph" (Fig. 51).

This model differs from that depicted in Fig. 50, in that the direct writing sphygmograph lever is connected with but a single pneumatic recording mechanism.

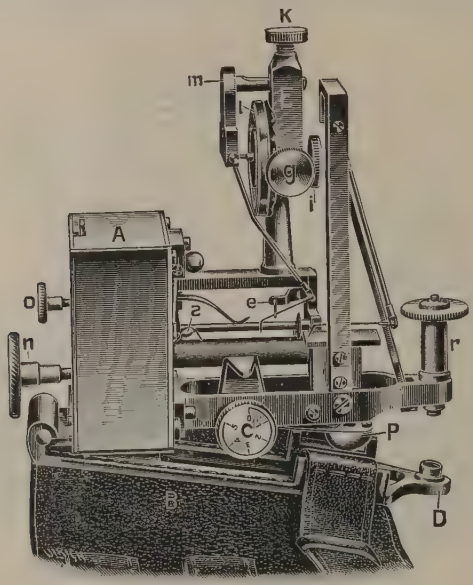


Fig. 51.—Simplified Jaquet's sphygmograph.

This instrument is, therefore, not only cheaper, but more compact and easier to manipulate; if the directions upon pp. 152 et seq. and p. 193 be followed, three or even more movements may be chronometrically compared with one another, although but two curves can be recorded simultaneously. For further information in reference to technic and to the significance of simultaneous records the reader is referred to p. 152 et seq. and p. 193, and also to the chapter upon Cardiography. This simplified cardiosphygmograph is also well adapted to the acoustic marking of the cardiac sounds, and to the recording of pneumatic signals upon sphygmographic curves, as is done in the determination of the minimum arterial pressure (p. 174).

The *Mackenzie polygraph* (Fig. 52) fulfills the same purpose as Jaquet's simplified sphygmograph, since it directly records the radial pulse and pneumatically records a second movement (carotid pulse, venous pulse, apex-beat, respiration, etc.). The sphygmograph employed in this instrument is Dudgeon's (p. 120). The pneumatic compartment, constructed like the ordinary Marey's drum, may be inserted at the point *b* in a movable upright.

This appliance has also been utilized by the author for the acoustic marking of

the cardiac sounds and for the recording of signals in the determination of the minimum arterial pressure (p. 174). In the figure is depicted one of the beaker-like receiving appliances, such as is employed by Mackenzie, instead of the small glass funnel. For the recording of hepatic pulsations Mackenzie employs a similar receiving appliance of larger size, which is pressed deeply into the hepatic region. In order that the writing-lever be not elevated too far above the writing surface,

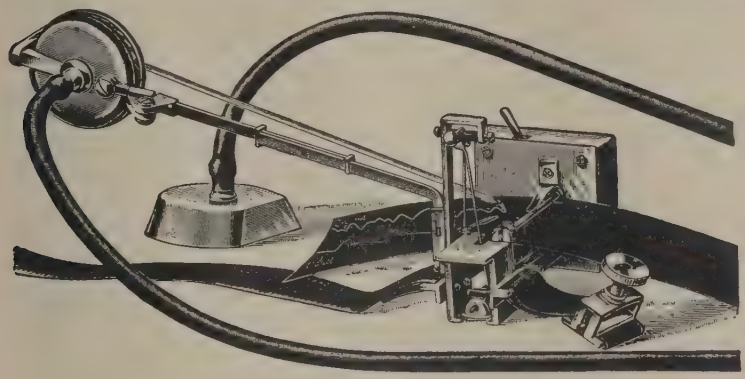


Fig. 52.—Mackenzie's polygraph and recording mechanism.

the larger receiver is provided with a lateral opening, which is left open when the receiver is pressed against the area in order to let the air escape, and then closed with the finger during the recording of the curve.

SIGNIFICANCE OF A NORMAL PULSE-CURVE; FACTORS WHICH INFLUENCE ITS FORM

The curves obtained with the good modern sphygmographs usually correspond quite uniformly. Fig. 53 represents a normal pulse-curve of the radial, the artery which is commonly selected. This illustrates what we have already learned from palpation, that the pulse-wave is composed of a steep ascending and a rather slanting descending limb. Palpation alone might lead us to believe that the ascending and descending limbs of the wave present smooth lines, but sphygmographic tracings show a number of small elevations in the descending limb (so-called catacrotic elevations). Similar irregularities which may appear under pathologic conditions in the ascending limb are termed *anacrotic* elevations. A pulse with catacrotic elevations is termed *catacrotic;* one with anacrotic elevations, *anacrotic.*

The normal pulse has usually three distinct catacrotic elevations, and is therefore catatricrotic. The significance of the individual parts of the pulse-curve, especially of these elevations, has created much discussion. Marey and Landois, and recently Hürthle, v. Frey, and Krehl, have taken the most active part.

To understand the pulse-curve we must, first of all, avoid confusing the progressive motion of the blood with the wave motion. This difference is very clearly illustrated by E. H. Weber's well-known expression, "Unda non est materia progrediens sed forma materiæ progrediens."

In palpating a pulse or in employing a sphygmograph we study exclusively the wave motion of the blood. Of course, the wave motion has some connection with the conditions of the blood-current, but only

indirectly. The pulse of a peripheral artery is a wave motion which has reached this vessel by transmission to the periphery of the primary wave arising in the aorta, long before the blood whose impulse produced the primary aortic wave has reached the artery. The rate of transmission of the wave motion of the blood is quite rapid—according to E. H. Weber about 9 m. a second. As we should expect, from what has just been said, an aortic curve (from an animal) corresponds very closely to the human radial curve. It rises quickly, and falls off gradually with secondary waves and depressions. To understand the radial curve thoroughly, it is well to begin by analyzing the aortic curve. The wave motion in the aorta is evidently due to the fact that during the "expulsion period" of systole the blood-content of the aorta is increased. Afterward, when the aortic valve has closed, this increase is carried toward the periphery by the increased tension of the aortic wall. Thus the ascending limb of the aortic curve evidently corresponds in general to the so-called "expulsion time," *i. e.*, the period during which blood flows from the heart into the aorta. The summit of the pulse-curve, however, does not correspond exactly to the end of the "expulsion time," *i. e.*, to the closure of the semilunar valves. On the contrary, the "expulsion time" is probably extended over into a part of the descending arm of the curve, because the flow of blood into the aorta is

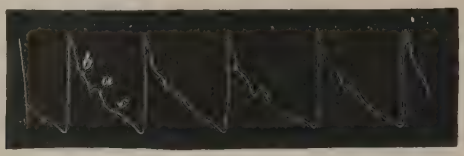


Fig. 53.—The normal radial pulse-curve (Riegel).

being diminished, so that the aorta is being partially emptied toward the periphery all the time. The end of systole is, then, not marked in a pulse-curve, but lies in the descending limb of the curve, somewhere near the summit. The descending limb of the curve thus includes this remnant of the "expulsion time" plus the whole period during which the aortic valve is closed, *i. e.*, that part of systole which lasts after the close of the semilunar valves (Martius "persisting interval"); the whole of diastole; and the so-called "closure time" of systole.[1] Hence, the descending limb is more than diastolic; but for the sake of brevity it may be called diastolic.

The secondary elevation of the descending limb, which is designated *a* in Fig. 53, is usually distinguished from the others by being very distinctly marked. If it be still further developed, the pulse becomes dicrotic. It is, therefore, called the "dicrotic elevation or wave," and is generally considered to be a "recoil elevation," coinciding with Landois' theory of its origin, which, however, will not withstand criticism. His theory is as follows: At the moment when the primary positive wave leaves the aorta, *i. e.*, when the stretched aortic wall, in virtue of its elasticity, retracts again, this elastic retraction exerts an impulse upon the column of blood. This impulse strikes the closed aortic valve, is reflected back, and passes through the aorta centrifugally

[1] [See Robinson and Draper, "The Presphygmic Period of the Heart," Arch. Int. Med., 1910, vol. v, No. 2, p. 168.—Ed.]

to all the peripheral vessels in the form of a second positive pressure wave. In cases where the duration of each pulse-wave is sufficiently long for a complete formation of the pulse-curve, the recoil wave may, in its turn, according to Landois, produce another second recoil wave. This second recoil elevation may be recognized by the fact that it follows about as quickly after the recoil elevation as the latter did after the primary wave.

Landois considers that *b* and *c* (Fig. 53), which are smaller elevations, are elasticity elevations, *i. e.*, due to individual vibrations of the arterial wall which are not transmitted from the blood-column to the arterial wall, but, conversely, from the arterial wall to the blood-column. (See p. 132 et seq. for a criticism of this conception of the secondary elevations.)

From experiments with rubber tubes Landois[1] states the following laws governing both kinds of secondary elevations:

1. The further the artery is from the heart, the later the recoil elevation appears in the diastolic portion of the curve.
2. In the same artery, the further from the heart we apply the sphygmograph, the less pronounced is the recoil elevation.
3. The recoil elevation is so much the more pronounced at the heart the shorter (sharper) the primary wave, and vice versâ. The duration of the primary wave being equal, one of large volume produces a stronger recoil wave than one of small volume. If, however, such a large voluminous wave persist for some time, while a small wave last only a short time, the latter will produce the larger recoil elevation. The deciding factor is thus always the brevity, *i. e.*, the celerity of the primary wave.
4. Other things being equal, the recoil elevation is larger the lower the mean arterial pressure.[2]
5. The further the examined artery is from the heart, the more marked are the elasticity elevations in the descending limb of the curve.
6. An accentuation of the mean pressure in the artery will increase the number of the elasticity elevations upon the descending limb, and at the same time bring them nearer the summit of the curve.
7. When the mean blood-pressure is very low, the elasticity elevations disappear entirely.
8. In diseases of the vessels which affect or destroy the elasticity of the artery, the elasticity elevations are either much diminished or else disappear entirely.

The following assertions may be ventured in regard to the varying shapes of the entire curve.[3] They are based partly upon experimental investigations by Marey, Landois, and others with tubes, and partly upon clinical observations:

1. Other things being equal (the same blood-pressure), the pulse-curve is higher the larger the systole, and vice versâ.
2. Other things being equal (equal systole and equal blood-pressure), the ascending limb of the curve is steeper the more quickly systole takes place.
3. Other things being equal, a low mean blood-pressure produces both a steep ascent and a steep descent, *i. e.*, a pointed curve (celerity of curve *in toto*). Conversely, a high blood-pressure produces a slanting rise and gradual descent (tardiness of curve).

[1] Die Lehre vom Arterienpuls, 1872.

[2] Attention must here be called to the fact that while this is generally true, we are by no means always justified in assuming the existence of low blood-pressure from a distinct development of the so-called recoil elevation, better termed the dicrotic wave. The author was convinced of this by the following experiment upon a dog: A sphygmogram was made from the exposed femoral artery and the pressure in the other femoral artery simultaneously measured by a mercurial manometer directly connected with the vessel. The arterial pressure was enormously increased by an injection of strychnin, and in spite of this the sphygmogram exhibited the most pronounced dicrotism. The subsequently stated view of the limited clinical value of the form of the sphygmogram might be based upon this experiment.

[3] A very good way of judging the real shape of a curve with many secondary elevations is to bisect each secondary elevation and then join the points by a dotted line, as in Fig. 54.

4. Other things being equal, rigid arterial walls (like high blood-pressure) produce low curves with slanting ascent and gradual descent (tardiness). On the contrary, delicate elastic arteries (like low blood-pressure) produce curves with steep ascents and descents (celerity).

As a matter of clinical experience, however, it must be acknowledged that only the descending limb of the curve is affected by either arterial rigidity or blood-pressure, for the great working capacity of the heart is sufficient to make the rise of the curve steep even with rigid arteries and with a high blood-pressure. All these statements possess more theoretic than diagnostic interest.

Anacrotic elevations occur only under pathologic conditions. Landois has come to the following conclusions concerning them:

Anacrotic elevations, *i. e.*, secondary elevations in the ascending limb of the curve (Fig. 68), are elasticity elevations. They depend upon influences similar to those which cause the ordinary elasticity elevations of the descending limb. The reason that anacrotic elasticity elevations are so rarely observed is because, as a rule, the ascending limb is so steep that elasticity elevations could not be reproduced in it. Hence, all the factors which tend to retard the rise of the curve are capable of producing anacrotic elevations, especially when these factors referred to also favor the formation of elasticity rises. (See above and p. 148.)

The shape of the curve is decidedly influenced by the frequency of the cardiac action, because a quick sequence of the chief wave makes a complete formation of secondary waves in the descending limb impossible. At the moment that the systolic rise of a new wave begins, all secondary elevations disappear in the great rise

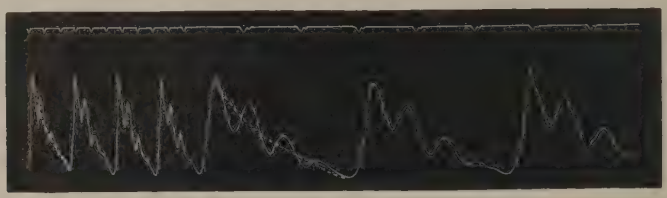


Fig. 54.—Reduction of a sphygmogram to its simplest form. The above curve was taken with a Jaquet's instrument, the four waves at the left while the paper was moving slowly; the three at the right while moving rapidly. The time intervals are shown in the notched line above (0.2 second).

of the new wave; although otherwise they would have developed in the descending limb of the preceding wave. Curves with a slow sequence of beats are, therefore, generally richer in secondary elevations. An illustration of the action of the frequency of beats upon the pulse-wave is the change of a febrile dicrotism of the pulse to hyperdicrotism and to monocrotism. (See Fig. 70.)

Although these facts are essentially correct, the explanations mentioned are not necessarily so, and they consequently do not possess any considerable clinical value, because, as stated in the preceding paragraphs, the form of the sphygmogram always depends upon different factors which, clinically, cannot be sufficiently analyzed. All these statements, however, are still encountered in the literature and are responsible for false deductions from the sphygmogram. Landois' explanation of the secondary elevations favors such false deductions, for it is incorrect, although not generally recognized. Von Frey and Krehl disproved it. These investigators studied the pressure curve by an artificially produced current impulse upon an aorta (left *in situ*) in a recently killed animal. They registered simultaneously the manometric pressure curve from the beginning of the aorta and from the celiac axis. A detailed examination showed that each individual secondary elevation may be explained by the fact that the primarily produced variations in pressure are reflected, as it were, from the periphery to the center and then back again to the periphery. Under certain conditions they may traverse

this path repeatedly in the curve. According to this there are neither recoil nor elasticity elevations; the so-called waves (even the anacrotic elevations) are nothing more than centripetal or centrifugal reflections of the principal wave, which interfere with it in various ways as well as with one another. Von Frey and Krehl claim that these elevations, and especially the dicrotic rise in every vascular area, are due to centripetal and centrifugal impulses, but in different and complicated ways. They characterize the dicrotic rise practically as a reflected wave which arises late, and which is, therefore, very distinctly marked from the main wave; whereas, they characterize the so-called elasticity waves which precede the dicrotic rise merely as waves derived by reflection of the main wave from points closer together, so that they are partly confluent with the main wave. Further, they characterize the elasticity elevations which come after the dicrotic rise as waves of reflection, like the latter, but arriving late and becoming less and less distinct toward the end of the curve, because the distance they traverse progressively increases.

According to these views, which are undoubtedly correct, the terms "recoil" and "elasticity elevations" must finally be omitted from clinical terminology, just as was the case with the expression "valve-closure elevation," which also depended upon a false conception, and has now happily disappeared from the literature. Because these designations are still current in the literature, and because their present omission would result in confusion in a general book such as this, they are retained here, much to the author's regret.

The next question is, will these theories explain the relationship between the height of the blood-pressure and the so-called elasticity elevations and the dicrotic waves—a relationship which possesses a certain although a limited importance? But von Frey and Krehl found that an increase of the blood-pressure pushed the reflected waves nearer to the main summit of the curve (*i. e.*, in the sense of time), because the rate of transmission of the waves increases with the blood-pressure. This explains the fact that those reflection waves which are situated nearest to the main summit (which are ordinarily described as elasticity elevations), and which include the anacrotic elevations, occur chiefly when the blood-pressure is high. It also explains the fact that with a low blood-pressure a reflection wave occurs as a so-called dicrotic wave arriving very late and characterized by being very distinctly formed, because at this moment the tension of the arterial wall is low enough for the wall to make quite a marked excursion. So we see that, as a matter of fact, these relations between blood-pressure and the form of the curve may be explained by the theory of the reflection of the secondary elevation.

The Negative Sphygmogram as a Source of Error

A comparatively little known source of error in sphygmography, to which Mackenzie[1] first called attention, is that an inverted curve is sometimes obtained.

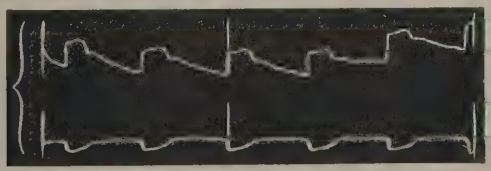


Fig. 55.—Mackenzie's negative sphygmogram. Two curves taken from the carotid simultaneously. The receptor of the upper curve was upon the artery, that of the lower was laterally placed. The lower curve is almost the reverse of the upper one.

When the radial or carotid, for example, pursues a tortuous course, its form is so

[1] The Study of the Pulse, 1902.

changed at the moment of maximum pressure that the tortuosity is diminished and the artery consequently moves laterally. If the pelotte of the sphygmographic appliance be not exactly upon the middle of the artery, it can happen that the sphygmograph records this lateral movemen, instead of the blood-pressure, and if the pelotte be so placed that the artery is removed from its pressure by the pulse-wave, there may be produced what Mackenzie has designated as a *negative sphygmogram.* (See Fig. 55, which is a pronounced example.) It was formerly believed that such a plateau-shaped pulse was produced by too strong a tension of the spring or, as it was sometimes expressed, it was "mashed." This conception, however, is entirely erroneous.

The Influence of the Respiration Upon the Pulse-curve

To study the influence of the respiration upon the pulse-curve, it is necessary to have simultaneous graphic records of the radial pulse and of the respiration. The least complicated instrument for this purpose is the simplified Jaquet sphygmocardiograph, as depicted upon p. 128, a combination of the Jaquet sphygmograph with a pneumatic appliance by means of which another movement can be recorded upon the same strip of paper. The small funnel which serves as a pneumatic receptor (see p. 128) is applied either to the jugulum or to the supraclavicular fossa. (See p. 100.)

It has long been known that deep breathing may have some influence upon the pulse-curve. This influence is chiefly due to the changes of arterial pressure which occur in the two phases of respiration. The respiratory increase in pressure manifests itself in a sphygmogram by an elevation of the whole curve[1] and by an alteration in the shape of the individual pulse (the latter corresponds to what was said in 4 and 6, p. 131 et seq.), viz., a diminution of the dicrotic rise, an increase of the elasticity elevations.

Authors differ very materially, however, as to whether the variations in pressure which are evident in a sphygmographic tracing belong to inspiration or to expiration. The reason for such a difference of opinion is that the factors which alter the blood-pressure during respiration are manifold; they frequently produce opposing results, and the final effect varies according to the way that the breathing progresses. The most important influence of breathing upon the blood-pressure is probably to be found in the change of diameter of the pulmonary vessels. They become wider during active inspiration and narrower during expiration.[2]

Consequently, so long as the dilating pulmonary vessels receive an excess of blood at the beginning of inspiration, the greater circulation must receive less blood (because the size of the diastole, and with it that of the systole, is diminished), and so the blood-pressure will fall. However, in the second part of inspiration the pulmonary circulation through the dilated pulmonary vessels improves; this in turn favors both diastole and systole, and eventually the greater circulation, and so increases the blood-pressure. During expiration the reverse occurs. The pulmonary vessels become narrower; they therefore empty a part of their blood into the greater circulation; the diastole and the systole of the left heart become fuller and the pressure increases. As soon, however, as the pulmonary vessels have become empty, the increased resistance in the lung will be felt as a factor in diminishing the diastole of the left side, and the pressure in the general circulation will be reduced.

Therefore, under these conditions blood-pressure falls during the first half and increases during the second half of inspiration; whereas, conversely, pressure increases during the first half and diminishes during the second half of expiration. Hence, a maximum of pressure occurs at the beginning of expiration; a minimum, at the beginning of inspiration. These rules, however, apply only to very slow and deep breathing. Only the initial effect of the change of diameter of the pulmonary vessels is felt during rapid breathing, viz., expiration increases the pres-

[1] This sign is, however, ambiguous, because the pelotte of the sphygmograph rests not only upon the artery, but also upon the venæ comites, and, of course, any increased dilatation of the latter will also lift the registering-levers.

[2] The conditions differ in the case of the artificial respiration employed in animal experiments.

sure, inspiration diminishes it. Hence, respiration influences blood-pressure in two opposite ways, according to its rapidity. And especially in pathologic cases, where the breathing is abnormal, it is evident that the two types may be merged beyond recognition, so that we are unable to formulate any fixed rule for the relation of the sphygmogram to the respiratory phases. This is one of the causes for the diversity of opinion found in literature. As a matter of fact, we have considered only the most important factor by which respiration affects the arterial pressure, namely, the varying diameter of the pulmonary vessels, whereas in reality the conditions are much more complicated; for example, we might consider the influence of the varying intrathoracic pressure upon the heart and upon the great intrathoracic vessels, the effect of varying intra-abdominal pressure upon the vessels of the abdominal cavity, which changes with respiration, and further the changes of the vasomotor tonus synchronous with respiration. Nevertheless, it may be stated, as a rule, that in the sphygmographic tracing (Fig. 56) deep and slow breathing increases the pressure during inspiration and diminishes it during expiration; whereas deep and rapid breathing produces the reverse effect. The pulse frequency is often accelerated during inspiration. Corresponding to the mode of origin of the variations in pressure, the individual beats which coincide with the increase in pressure are greater than those which correspond to its decrease.[1]

It should also be noted that the lower the arterial pressure, the more decided are the effects of respiratory influence upon the pulse-curve, since thoracic aspiration naturally causes a greater increase of arterial pressure when the arteries are

Fig. 56.—The influence of deep and slow breathing upon a normal pulse-curve: *R*, Respiration curve, inspiration upward; *P*, pulse-curve; *T*, time curve (intervals = 0.5 second) (Rollet).

comparatively empty than when they are markedly full. Such imperfect filling of the arteries generally, but not always, coincides with low pressure. Upon the other hand, with a low arterial pressure the arteries may be even abnormally distended, *e. g.*, when the low pressure depends upon dilatation of the arteries with a good volume of circulating blood. Arterial pressure in itself is consequently not responsible for the occurrence of pronounced respiratory variations in the pulse-curve, but for the volume of blood contained in the arteries. To this extent the occurrence of marked inspiratory variations in the pulse-curve possesses a certain interest in our consideration of circulatory conditions.

It must always be borne in mind that the pulse-curve may be affected by abnormalities of breathing, for disregarding the previously mentioned effect of the frequency, the influence of respiration upon the pulse-curve is naturally more pronounced if the respiration produce great variations in intrathoracic pressure. As a result of this we observe particularly pronounced variations of the pulse-curve in stenoses of the air-passages and in all conditions, like pneumonia and pleurisy, in which the equalization of the intrathoracic and extrathoracic air pressures is disturbed.

Mackenzie (*loc. cit.*) gives two interesting examples of simultaneous records of the respiration and of the pulse (Figs. 57 and 58). Fig. 57 is a record in which the respiratory period accidentally corresponds in length with the period of a trigeminal pulse, so that without a simultaneous graphic record we might be led to suppose

[1] For further information see Tigerstedt, Lehrbuch der Physiologie des Kreislaufes, 1893, p. 453 et seq.

that the causal factor of the trigeminal pulse was to be found in the respiration. The simultaneous record shows, however, that the respiratory curve holds a constantly changing relation to the period of the trigeminal pulse, and such a direct causal relation may thus be excluded. Figs. 58 and 59, exhibit sphygmograms from the arm, in which the involuntary movements of the arm dependent upon respi-

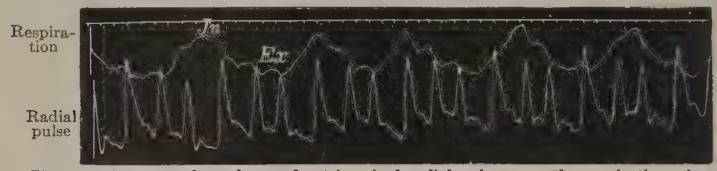


Fig. 57.—Apparent dependence of a trigeminal radial pulse upon the respiration, since the duration of the periods of the trigeminal pulse coincides with the duration of the respiratory periods (Mackenzie, *loc. cit.*, p. 163, Fig. 157). Such a direct dependence does not exist, however, because the phase of the pulse variations is constantly displaced in its relation to the respiratory curve.

ration simulate the influence of the respiration upon the pulse-curve. Fig. 58, which seems to demonstrate the marked influence of the respiration upon the pulse-curve, was taken when the arm was not fixed; Fig. 59 was recorded with the arm firmly fixed, and such influence is almost entirely wanting.

Respiration exerts a particularly pathologic influence upon the pulse-curve when, as the result of intrathoracic adhesions (particularly in the mediastinum),

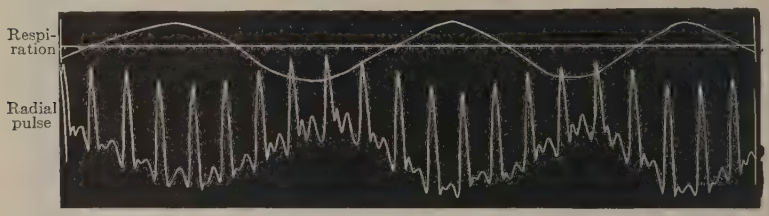


Fig. 58.—Variations in the pulse synchronous with the respiration (copied from Mackenzie, Fig. 158, p. 164).

inspiration or expiration exerts an abnormal traction or pressure upon the veins leading to the heart, by which the blood is more or less withheld from the vessels during one of the respiratory phases (pulsus paradoxus, cicatricial mediastinitis, see p. 143 et seq.).

Besides the effects of the previously mentioned mechanical and direct influences upon the circulation, we must also bear in mind an indirect influence of the respira-

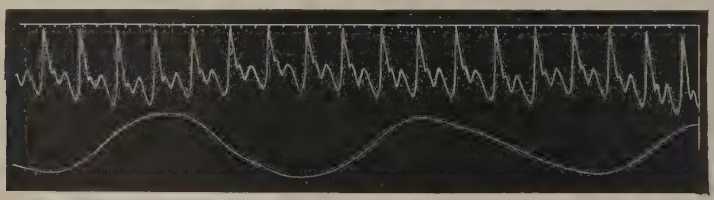


Fig. 59.—The same pulse with the arm fixed, copied from Mackenzie (Fig. 159, p. 164). The variations in the pulse which were synchronous with respiration have almost entirely disappeared. The variations in the pulse-curve are consequently largely dependent upon the movements of the arm associated with respiration.

tion upon the cardiac and vascular innervation. Certain disturbances of rhythm, such as the occurrence of extrasystoles, for example (see p. 154 et seq.), may consequently be associated with definite respiratory phases or at least repeat themselves in the respiratory tempo. Upon this point, however, there is little known. The case recorded in Fig. 57 also belongs under this head.

Under normal conditions the influence of respiration upon the pulse-curve is slight and scarcely perceptible even in the sphygmogram, so that when marked inspiratory variations are present in the pulse-curve, we should look for one of the above-mentioned pathologic factors.

OTHER FACTORS WHICH INFLUENCE THE PULSE-CURVE

1. Diminution of the amount of blood. This produces a diminution and a delay in the elasticity elevations and a decided prominence of the dicrotic wave. Phlebotomy may sometimes be sufficient to accomplish this effect.

2. An intermitting cardiac activity diminishes the arterial pressure during the intermission of the pulse. Consequently the pulse-wave following upon the pause presents signs of diminished pressure, *i. e.*, the elasticity elevations are weaker and delayed and there is more pronounced dicrotism.

3. Elevating an extremity diminishes, depressing it increases, the arterial pressure in the part, as a result of the hydrostatic effect of the pressure of the column of blood in the particular artery. Consequently the sphygmogram of an elevated area shows more distinct dicrotism and slighter elasticity elevations than that of a horizontal or dependent area.

4. Compressing the larger vascular trunks produces an increase of pressure in the other pulsating vessels. This is shown in a well-known way by the sphygmogram.

5. An interference with the venous flow from an extremity acts in an opposite way. The arterial pressure in the supplying artery increases, and its sphygmogram is correspondingly altered. The rise of the curve as a whole is, however, partly due to the distention of the congested veins. (See p. 135, Note 2.)

Landois and Marey are responsible for most of these statements.

DIAGNOSTIC SIGNIFICANCE OF THE PULSE-CURVE

At first observers were naturally inclined to overestimate the value of sphygmographic tracings for the diagnosis of pathologic conditions, but to-day most clinicians have gone to the opposite extreme. As a matter of fact, sphygmography is more than an interesting amusement: it is really a valuable help in the interpretation of circulatory changes.

THE EMPLOYMENT OF THE CONTINUOUS TOTAL SPHYGMOGRAM

While many difficulties are encountered in drawing conclusions from the form of the individual pulse-curve in the sphygmogram, the employment of the pulse series therein is much less objectionable, as may be seen from the following sections upon the frequency and the rhythm of the pulse, from the "practical examples" (p. 149), and from the special section upon the analysis of the arrhythmic pulse (p. 152).

FREQUENCY OF THE PULSE IN THE SPHYGMOGRAM

With Jaquet's and with von Frey's latest sphygmograph, both of which are furnished with a time-marking apparatus, we can estimate the frequency of the pulse very accurately merely by the sphygmographic tracing. It should, nevertheless, be noted that in certain cases errors may occur in estimating the pulse frequency, even from the sphygmogram, unless auscultation, cardiography, and the recording of the venous pulse be also employed. Examples: Pseudobradycardia (see Bradycardia, p. 113 et seq.) and the pulsus pseudoalternans (Fig. 63, p. 142). The sphygmogram, best combined with the venous pulse tracing, is of especial importance in an explanatory analysis of such exceptional alterations in frequency as *tachycardia* and *bradycardia*. (See p. 157 et seq.)

RHYTHM OF THE PULSE IN THE SPHYGMOGRAM

A pulse-tracing shows the pulse rhythm at a glance, and much more accurately than it can be described. A *regular* pulse is one in which the individual waves follow each other at exactly equal intervals of time. Where this is not the case, the pulse is termed *irregular*. If the irregularity be complete, we call it a *pulsus irregularis*, without further comment. A *pulsus intermittens* is one in which, after a regular number of waves, one beat from time to time is omitted. A *pulsus intercidens* is one in which a small beat is inserted into a regular sequence of beats. The so-called *bigeminus* (Figs. 60 and 76) and *trigeminus* (Fig. 61) rep-

Fig. 60.—Pulsus bigeminus in typhoid fever; due to extrasystoles (Jaquet's sphygmograph, model II, p. 124).

resent periodically irregular pulses. In the former 2 beats, and in the latter 3 beats, are grouped together and separated from the preceding and following beats by a somewhat longer interval. Their curves usually do not reach the base line between the groups of 2 or 3 beats, so that the sphygmogram looks like a two- or three-peaked curve.

The designations just employed express only the apparent form of the pulse. With the exception of the failure of a pulse from disturbances of conduction (see p. 157 et seq.), auscultation demonstrates that the intermittent pulse is due to extrasystoles, *i. e.*, to supernumerary systoles, brought about by abnormal or so-called extra stimuli, which are so closely approximated to the normal systoles that they do

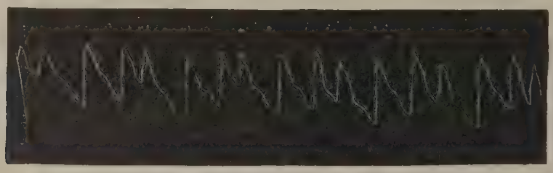


Fig. 61.—Pulsus trigeminus equalis (after Riegel) (extrasystoles).

not produce a pulse in the peripheral artery, since at this time the heart is insufficiently filled. The pulsus intercidens is also to be regarded as an extrasystole introduced into a regular pulse-wave and transmitted to the periphery. Most instances of pulsus bigeminus and trigeminus (except the characteristic grouping from conduction disturbances, p. 157 et seq.) are likewise to be regarded as the result of extrasystoles, since one (bigeminus) or two (trigeminus) such extrasystoles are so interpolated into the main pulse that they are also apparent in the peripheral artery.

In reference to the occurrence of the different irregularities of rhythm see chapter upon the Modern Analysis of the Irregular Pulse (p. 152 et seq.). In reference to the

possibility of distinguishing a competent from an incompetent heart by making use of the sphygmographic form of the irregularity see p. 149 et seq., under Practical Examples.

THE EMPLOYMENT OF THE CURVE OF THE INDIVIDUAL PULSE

The chief difficulties in the interpretation of the sphygmogram are encountered in the curve of the individual pulse. The factors which influence the shape of the individual pulse-curve are so numerous (see p. 131 et seq.) that many different circulatory conditions may be responsible for an identical sphygmogram; so that even in a cardiac case we are not justified in making a diagnosis merely from the type of the curve. Even the curve of aortic insufficiency, one of the most characteristic of all curves, cannot be considered as pathognomonic of this affection; exactly the same type may occur without any valvular lesion. Still, the sphygmogram is valuable in the diagnosis of many conditions, provided that other symptoms are given their proper value, and provided that the clinician possesses considerable technical skill in making the tracings and a very accurate knowledge of the significance of the sphygmographic curve and of the way it may be modified by various factors. Such a knowledge can be obtained only by studying works upon physiology.[1]

One of the main objections to making use of the curve of the individual pulse for diagnostic purposes has been that all the variations in this curve attributed upon p. 131 et seq. to the arterial tension in the aorta, *i. e.*, to general circulatory conditions, can be produced by local changes in the vasomotor tone of the artery. Of course, if this objection were correct, sphygmography would practically be relegated to a useless place. Mosso is chiefly responsible for this objection. He found that the pulse-curve could be changed by local thermic application, *e. g.*, the local application of heat to the arm dilates the vessels and produces a pulse-curve characteristic of low tension, while local cold produces a curve characteristic of high tension. But a closer examination of Mosso's curves shows that such changes are quantitatively quite insignificant, and apply much more to the height of the curve than to its shape. Variations in the pressure acting upon the vessels from without produce but an insignificant effect upon the shape of the pulse-curve. This Mosso easily determined in his investigations, which were made with a water sphygmograph. The author has become convinced that it is extremely difficult to alter very materially the shape of the individual beats by such local thermic influences, either in the sphygmogram or in the tachogram.[2] Besides, where the changes are pronounced, it is not possible to exclude the effect upon the general blood-pressure which can be produced reflexly by the local application of heat or cold. In fact, where the greatest alterations were observed the patients reacted to the thermic changes with sensations of heat and cold. The author has never been able to change a high tension to a dicrotic pulse, or the reverse, by purely local influences of so moderate

[1] Landois, Die Lehre vom Arterienpuls, 1872; Marey, La Circulation du Sang, 1881; Grashey, Die Wellenbewegung elastischer Röhren und der Arterienpuls des Menschen, Leipzig, F. C. W. Vogel, 1881; v. Frey, Die Untersuchung des Pulses, Berlin, J. Springer, 1892; Mosso, Die Diagnostik des Pulses in Bezug auf die localen Veränderungen desselben, Leipzig, Veit & Co., 1879.

[2] E. Balli, Ueber den Einfluss von Erwärmung und Abkühlung der Haut auf das Flamentachogramm, I. A. D., Bern, 1896.

a degree that a general influence could at the same time be excluded. The general character of the pulse-curve remains the same even after a more extensive application of heat or cold to the arm. The difficulty in influencing the character of the curve is well illustrated by making tracings with a different amount of pressure upon the spring. Although the height of the curve as a whole, and that of the secondary curves, will be influenced, neither the general shape of the curve nor the number and position of the secondary elevations will be affected in the least. This remains true even if the artery be almost compressed at the periphery, and such a compression would apparently be quite similar to the effect of a sharp vasomotor contraction there. This fact convinced von Frey that the best way to employ the sphygmograph was with a very strong pressure of the spring, thus avoiding any excessive swinging of the registering lever. The more frequently and carefully one employs the sphygmograph, the more one is convinced that it registers the condition of the general, *i. e.*, the aortic, circulation, and that it is but slightly influenced by local vasomotor influences. The sphygmogram is, first of all (and herein lies its clinical value) the expression of the form which the pulse-wave assumes under the circulatory conditions of pressure and resistance in the aorta and its large branches. Another thing worth remembering is this, that excessive vasomotor conditions, such as Mosso employed (local baths, violent muscular motions, etc.), rarely affect the ordinary radial beat. If they did we should notice other evidences of vasomotor action, such as an increased temperature or redness of the skin. The radial vasomotor tonus of an individual ordinarily clothed and reasonably quiet in all probability varies but little from the average value, which depends upon the condition of the general circulation.

One practical difficulty with the sphygmograph is that in one case, even under physiologic conditions, the curve of the individual pulse may present several peculiarities which in another case would signify some pathologic variations. Hence, a sphygmogram is more practically useful in following the circulatory conditions in the same patient, *i. e.*, for what might be termed functional diagnosis of circulatory disturbances, than for ordinary diagnostic purposes. It is of decided assistance in studying more closely the therapeutic action of certain measures upon the circulation and of determining the more rational plan of treatment in a given case. Jaquet's sphygmograph is especially suitable for such comparative investigations, not only because an accurate time-recording apparatus is attached, but also because the amount of pressure upon the spring can be exactly reproduced each time. Another advantage is that the examiner can make at each trial five different curves (corresponding to the five degrees of tension in the spring, and so compare them with five others). This will prevent misjudging rather insignificant local variations of vasomotor tension. The increased pressure on the spring evidently has the same effect on the circulation of the hand as a marked increase of tonus of the radial artery. After a little practice one can take five such tracings very rapidly. There is still quite a difference of opinion whether high or low curves present the more correct picture. While the novice will a priori prefer high curves, attracted by the inappropriate construction of sphygmographs which give excessive swinging, see Dudgeon's sphygmograph, p. 120, the expert points out that these high curves are deformed by excessive

swinging and that it is better to choose the pressure giving a curve of moderate height. Since the modern instruments (Jaquet's sphygmograph, Model I, II, and III) do not permit much swinging, the high curves seem rather more suitable, because they show that the sphygmograph was very perfectly applied, and because their results are perhaps better for comparison in different patients as well as in the same patient. It is evident that the excursions of the registering-needle will be the highest when the tension upon the spring either just balances or is but very slightly in excess of the average pressure in the artery. (See p. 117.) On the one hand, this is because the transmission of the systolic increase of pressure to the sphygmograph is least interfered with by the relaxed arterial wall; and, on the other hand, because the next wave will back up considerably, and consequently the rise will be magnified, just as with a hydraulic press. Comparing the various pulse-curves with one another, especially under those well-definable conditions and with a perfect sphygmograph, is really very valuable.

VOLUME OF THE PULSE IN THE SPHYGMOGRAM

According to our definition on p. 118, the volume of the pulse is represented by the height of the primary curve summit above the base of the curve. Other things being equal, it is evident that the volume of the pulse depends upon the amount of blood which is thrown into the artery during systole. If this systolic amount of blood be the same, the volume of the pulse then depends upon the facility with which the arterial wall and the pelotte of the sphygmograph give way to the wave motion of the blood, *i. e.*, on the one hand, upon the passive tension of the artery as determined by the blood-pressure, and, on the other hand, upon the active tension of the muscularis of the artery and upon the tension of the spring of the sphygmograph. The volume of the pulse, *i. e.*, the height of the sphygmographic curve, also depends very decidedly upon the size of the surface of the artery (according to Pascal's law of the hydraulic press). With the same strength of systole of the left heart and the same blood-pressure, the larger the diameter of the radial artery, the higher the spring of the sphygmograph will be raised, and hence the larger the pulse. The frequency of the pulse also influences the height of the sphygmogram. If the pulse be rapid, a part of the descending limb of the curve will be cut off by the following wave. So many factors influence the volume of the pulse in ways which we cannot perfectly determine from the appearance of the curve itself, that the mere volume of the pulse is of very uncertain diagnostic significance. In the following cases, provided the tracings compared are all of a maximum height, the volume of the pulse is of some significance:

1. When the size of the individual beat varies in any one pulse-curve, we may be sure that the larger beat corresponds to a larger expulsion (*i. e.*, is preceded by a more complete diastole of the heart), and that the smaller beat corresponds to a smaller expulsion.

2. If the same patient's pulse become fuller and of lower tension when examined with the same sphygmograph (see pp. 131 and 146 et seq.), we are justified in assuming that a greater systolic expulsion is the cause.

On the other hand, if the full pulse be at the same time of increased tension, its increased size can be due only to the fact that with the increased resistance in the circulation and the resulting high blood-

pressure, even a smaller systole produces a marked increase of pressure in the arterial tube, which is already markedly distended and consequently less elastic. The reason for these statements will be found in the section upon Sphygmobolometry.

The following terms refer to the size of the pulse: *Pulsus equalis* and *inequalis* (the latter is usually a pulsus irregularis as well); *pulsus inequalis periodicus*. The most interesting types of the latter are the *pulsus alternans* (Fig. 62) and *pulsus paradoxus* (Fig. 64).

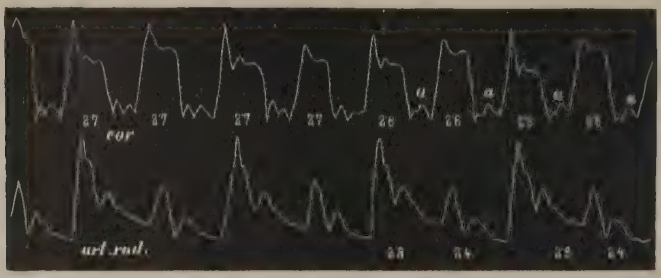


Fig. 62.—Pulsus alternans (Volhard).

By *pulsus alternans* we understand the alternate occurrence of a large and of a smaller pulse in an almost constant rhythm. The nature of this phenomenon and its differentiation from similar forms of the pulsus bigeminus is discussed upon p. 162.

The *pulsus paradoxus*, a poorly chosen name, was first described by Griesinger,[1] and later by Kussmaul, as a constant symptom of indurative mediastinitis. Its peculiarity is that during inspiration the pulse becomes feeble or else cannot be felt at all. Kussmaul explains it as due to an inspiratory pull upon the veins leading to the heart by the

Fig. 63.—An apparent pulsus alternans, which was shown, by counting the apex-beats and marking the cardiac sounds, to be actually a pronounced dicrotic pulse in which the small, interpolated wave is to be regarded as a dicrotic elevation (pseudotachycardia, see p. 113).

intrathoracic adhesions. From the explanation given on p. 134 et seq. it follows that this symptom can have no pathognomonic importance in the diagnosis of indurative mediastinitis. From the physiologic significance of the inspiratory diminution in the size of the pulse, as there explained, it is not surprising that it has been observed also in pericarditis, in valvular disease, in weak heart, in pneumonia, in pleurisy, and in stenoses of the air-passages (laryngeal and tracheal stenoses, obliterative bronchitis). Even when the heart and lungs are abso-

[1] Widenmann: Beitrag zur Diagnose der Mediastinitis, Tübingen, 1856.

lutely normal, it is possible that respiration may produce some evident effect upon the pulse, although this is not usually the case, as we have previously pointed out on p. 134.

It seems to the author that the pulsus paradoxus is of value in the diagnosis of indurative mediastinitis only when there is a concomitant inspiratory engorgement of the jugular veins, a symptom which indicates a stenosis of the jugular veins during inspiration.

The typical pulsus paradoxus (Fig. 63) is copied from Kussmaul's original communication. It especially seems to the author to possess no diagnostic importance whatsoever. As is easily seen from the figure, the pulsus paradoxus is just twice as frequent as the respirations, so that expiration always coincides with one beat and inspiration with the other. If the breathing be energetic, this relation will naturally emphasize the physiologic factors described on p. 134. As a matter of fact, the breathing is rapid, so that under the circumstances, according to p. 134, with each diminished filling of the arteries, the pulse shows more or less distinctly an inspiratory decrease or even a disappearance. Besides, from what has been mentioned on p. 134, it is evident that under certain circumstances, and practically independent of the frequency of the respiration, a noticeable diminution or even an omission of the pulse may be observed, even during expiration. Such a phenomenon might just

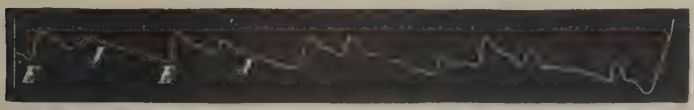


Fig. 64.—Pulsus paradoxus: *E*, *E*, Beginning of expiration; *J*, *J*, beginning of inspiration (Kussmaul).

as well be called a "pulsus paradoxus," and it certainly has just as little significance in the diagnosis of any definite disease.

Although all these phenomena of an alteration in the pulse from respiratory influences coincide with the occurrence of a low arterial pressure (p. 134), we are not justified in diagnosing from their presence any one definite disease, such as pericarditis or mediastinitis, but merely a deficient general peripheral circulation, *i. e.*, an insufficient arterial filling.

CELERITY OF THE PULSE IN THE SPHYGMOGRAM

The celerity of a pulse is a quality which we can appreciate by palpation (p. 115). It is also plainly represented in the sphygmographic curve by the more or less marked abruptness of the ascending and of the descending limbs of the curve, and is measured mathematically by the angle formed by these limbs. Both ascending and descending limbs of a *pulsus celer* are steep and the summit is sharp (Fig. 64). On the contrary, both limbs of a true *pulsus tardus* are sloping, the curve is flat and the summit blunt (Fig. 65). Either limb of the curve may exhibit the signs of celerity or tardiness, while the other limb either is not affected or may exhibit the opposite condition. In this case our description must include the character of each limb. For the method of determining by construction the shape of the general curve, or of the main summit in the case of polycrotic curves, see Fig. 54.

A variety of the pulse of aortic insufficiency is encountered in the older literature as the so-called Corrigan pulse, which, in addition to the general characteristics of celerity, exhibits another peculiarity in that an anacrotic notch is present near the apex of the ascending limb, which is frequently followed by a plateau. Such curves are evidently due, however, to the excessive swinging which was always present in the older sphygmographs.

The usual absence of dicrotism in aortic insufficiency is due not to the defect in the aortic valve, which thus accounted for the absence of the "recoil elevation," in the old erroneous theory of the dicrotic wave, but simply to the pronounced celerity, *i. e.*, to the marked diastolic fall of pressure which reduces the reflected waves to a minimum.

Fig. 65.—Pulsus celer in aortic insufficiency (Riegel).

The ascending limb in aortic insufficiency (Fig. 65) is steep because a large mass of blood is suddenly expelled from the distended left ventricle into the aorta; and the descending limb is also steep because, on account of regurgitation of the blood into the left ventricle, the negative stage of the wave is introduced abnormally rapidly. Conversely, the ascending and descending limbs of aortic stenosis are oblique; it is a typical *pulsus tardus* (Fig. 65). Here the rise as well as the drop of the curve takes place slowly because the systolic impulse is deadened and prolonged at the seat of stenosis. In relaxed vessels (*e. g.*, in fever) the rise as well as the drop is usually quick. (See p. 131.) The dicrotic febrile pulse is therefore usually a *pulsus celer* (Fig. 70). With high

Fig. 66.—Pulsus tardus in aortic stenosis (Strümpell).

arterial tension the descending limb of the curve is usually quite gradual and oblique (p. 132), since the blood flows away slowly on account of the great peripheral resistance. The rise is generally rapid and steep on account of the energetic cardiac action. This is the type of pulse which is usually observed in old people with arteriosclerosis (Fig. 67). Nevertheless a very decided degree of arteriosclerosis (Fig. 68) is generally accompanied by a gradual rise. This is probably due to the simple fact that with high blood-pressure the reflex waves (see p. 132) occur so soon that they coincide with the ascending limb of the curve and change its appearance without forming distinct secondary elevations. The rounding of the apex in Fig. 67 is explained in an analo-

gous manner. (See p. 148.) In nephritis (Fig. 69) the rise is steep and the descent slow, but the pulse differs from that of arteriosclerosis by the great number of secondary elevations.

Although the general shape of the sphygmogram gives some idea of the arterial pressure and the way the blood flows into the arteries, and from them to the periphery, yet neither the descent nor the ascent of the

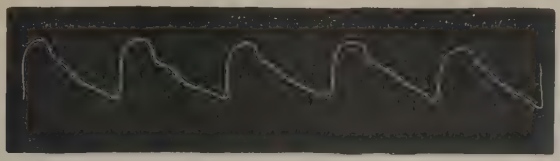


Fig. 67.—Senile pulse in arteriosclerosis (Riegel).

curve is absolutely diagnostic. In the first place, the height of the curve influences the slant of the descending limb; and, as a rule, we are unable to interpret the significance of variations in the height (p. 141). Again, the frequency of the pulse decidedly modifies the slant of the descending limb, because if a pulse be rapid, a portion of its descending limb is simply cut off by the following wave, so that the

Fig. 68.—Pulse in advanced arteriosclerosis: Slow ascent and descent of the wave; anacrotism—only 32 beats to the minute (taken with Jaquet's instrument).

height of the curve seems lessened. This naturally influences the form and the abruptness of the descending limb, since the retained portion of the descending limb seems abnormally steep when its concavity is directed upward and abnormally flat when its convexity is directed upward. Even in aortic insufficiency the value of the slant of the des-

Fig. 69.—Pulse in chronic nephritis.

cending limb is rather more for demonstration than for diagnosis. The slant of the ascending limb is almost as variable.

In order to exclude the height of the sphygmogram, which we have seen to be dependent upon many incidental influences, from our conception of pulsus celer and pulsus tardus, we should replace the expression "abruptness" of the limbs of the curve by the duration of the ascent and descent which may be actually measured by the sphygmo-

graph. This measurement is made by dropping a vertical from the apex of the curve to the abscissa, measuring the distances from the beginning of the ascent to the vertical line and from the vertical line to the end of the descent, and expressing these distances in time according to the unit marking. The celerity of the ascent or descent will then be inversely proportional to the periods of time. We must, of course, remember that the time interval of the ascending limb should not be confounded with the duration of the cardiac systole, for systole (p. 130) extends beyond the main elevation.

It should be observed that as a result of the fact that the duration of the ascent of the pulse-curve does not correspond with the duration of the delivery of the blood into the aorta, the demonstration of the characteristic pulse of aortic stenosis is frequently unsuccessful, since the duration of the ascending limb of the curve is shortened by the rapid flowing of the blood toward the periphery. The pulse simply seems small, but does not present the typical characteristics of the pulsus tardus. To the best of the author's knowledge, attention has not been previously directed to this evident explanation of the frequent absence of the pulsus tardus in aortic stenosis.

In conclusion, the author considers that a much more useful and accurate conception of celerity may be obtained from the use of the absolute sphygmogram (see p. 178) than from the preceding definitions.

TENSION OF THE PULSE IN THE SPHYGMOGRAM (POLYCROTISM; DICROTISM; ANACROTISM)

The secondary elevations of the descending limb (p. 131 et seq.) are most significant in attempting to estimate from the pulse-tracing the tension of the pulse, *i. e.*, the mean blood-pressure. Either elasticity elevations which are pronounced and which arise early in the curve (according to von Frey's and Krehl's conception (p. 133), the early reflex waves, *i. e.*, secondary elevations near the summit) or anacrotic elevations (p. 132) generally indicate a *high* mean blood-pressure. The converse, *i. e.*, the so-called dicrotic wave (p. 130), is usually more pronounced with a *low* mean blood-pressure (p. 131 and Note 2, p. 131). Where none of the secondary elevations, either from its size or its position, can be considered as a dicrotic wave, we are justified in assuming that numerous and pronounced secondary elevations are more in favor of a high pressure; because, according to Landois, these numerous elevations should be regarded as powerful, and, at least in part, early reflex waves.

(See p. 131 et seq. and p. 144 in regard to the general form and size of the pulse under variable mean pressure.)

Although exceptions frequently occur on account of the complicated conditions of wave reflection (see p. 133), the type of the pulse-curve with varying arterial pressure may be represented as follows:

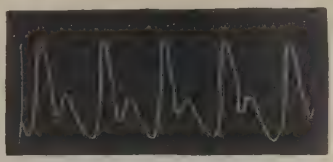
1. *Normal Pressure.*—Both the elasticity elevations and the dicrotic wave are moderately developed; the latter, however, differs very little from the elasticity elevations. (See Fig. 53.)

2. *Low Pressure.*—Elasticity elevations disappear, dicrotism increases, and eventually becomes transformed into monocrotism, *i. e.*, the pulse becomes a pulsus celer (Fig. 70, *b*, *c*, *d*, *e*).

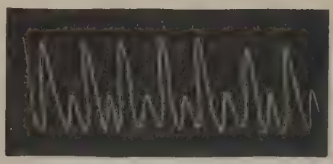
3. *High Pressure.*—Elasticity elevations increase in size and number; they are situated nearer the summit (Figs. 69 and 71) or even on the ascending limb of the curve (anacrotic); the descending limb, and in rare cases the ascending limb (see p. 144 et seq.), are oblique (tardus).

If the blood-pressure be very high, and especially if it be due to arteriosclerotic resistance, not only the dicrotic rise disappears, but even the elasticity elevations fade away more or less completely, because the arterial wall has become stiffened either on account of the firm contractions of its muscularis or on account of the arteriosclerotic changes. While this is the usual explanation of this phenomenon, it is perhaps more likely that it is due to the reflected waves being transmitted with such velocity that they disappear in the main apex of the curve. A monocrotic pulse finally results. Fig. 68 represents such a slow and almost monocrotic sphygmogram; but there still remain some indica-

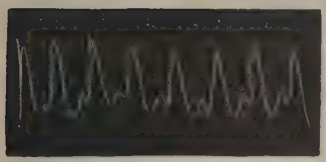
a. Normal with beginning dicrotism.



b. Hypodicrotism.



c. Dicrotism.



d. Hyperdicrotism.

e. Monocrotism.

Fig. 70.—Increasing dicrotism, finally transformed into monocrotism (Riegel).

tions of elasticity elevations visible especially in the ascending limb (anacrotism).

In this schematic grouping the relation of the celerity of the pulse-curve to the blood-pressure has only a theoretic significance, because the quality of celerity in the sphygmogram (pp. 141 and 145) possesses only slight diagnostic value.

In reference to the practical diagnostic significance of the tension of the pulse as a clinical expression of blood-pressure (see p. 173 et seq.) upon the diagnostic significance of the measurement of the arterial pressure.

Furthermore, merely counting the elasticity elevations is not always sufficient to determine the height of the blood-pressure, because the pulse frequency always plays a part. With a frequent pulse the curve is not completely developed, so that a part of the descending limb and the elasticity elevations contained in it will not show.

Under certain conditions pronounced dicrotism may simulate a pulsus bigeminus

or even a pulsus alternans (see Fig. 63, p. 142), just as, upon the other hand, an indistinct bigeminus from extrasystoles may simulate dicrotism and constitute pseudobradycardia. (See the curve of pseudobradycardia depicted in the section upon The Graphic Registration of the Cardiac Impulse.)

The development of a dicrotic wave is best studied in a febrile pulse, because dicrotism usually goes hand in hand with a diminution of the vascular tension. The higher the fever, the more fully the dicrotic wave is developed, and the further distant is it from the main summit of the curve (Fig. 70, *a*, *b*, *c*, *d*). The individual steps of this change have received separate names. If the dicrotic elevation begin before the descending limb reaches the base of the curve, the pulse is called *hypodicrotic* (Fig. 70, *b*). It is strictly *dicrotic* when the dicrotic wave starts only after the descending limb reaches the base line. If the dicrotic wave occur still later, *i. e.*, in the ascending limb of the following wave, the pulse is termed *hyperdicrotic* (Fig. 70, *d*). This peculiarity may arise either because the dicrotic wave is retarded or because the following wave, coming so rapidly, cuts off the descending limb of the dicrotic wave. If in Fig. 70, *c*, the ordinary dicrotic pulse, we imagine that the individual beats follow more closely one after the other, "hyperdicrotism" results (Fig. 70, *d*). If the dicrotic wave be still further retarded, or, what amounts to the same thing, if the rate of the pulse be still further increased, a monocrotic wave results (Fig. 70, *e*). This monocrotism with relaxed vessels and low pressure differs from the monocrotism of high pressure (Fig. 68). In the latter either the tense or rigid arterial wall cannot produce any considerable secondary elevations, or the secondary waves are reflected with such velocity that they become lost in the main apex of the curve. The pulse-wave is here usually tardus and the pulse very infrequent, probably because the heart is slowed by irritation of the vagus from high blood-pressure.

Mackenzie (*loc. cit.*) thinks that the old conception of sthenic fever may be best defined by the use of the sphygmogram. He believes that the marked development

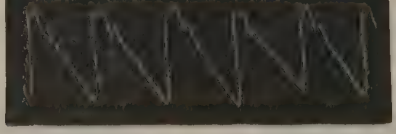


Fig. 71.—Tense pulse in lead colic: Some of the waves anacrotic (Riegel).

of dicrotism determines the character of sthenic fever (*i. e.*, favorable), while the slight tendency to dicrotism is equally characteristic of the asthenic or unfavorable fever pulse. He sees in the absence of pronounced dicrotism the sign of a low reserve of pressure during diastole, a low minimum pressure, that is to say, the sign of insufficient cardiac energy or of pronounced vasomotor weakness. Since we have seen, however, that the form of the pulse-curve is influenced by the frequency of the pulse, by the diameter of the artery, and by the application and peculiarities of the sphygmograph in a manner beyond all calculation, Mackenzie's conclusions in this respect cannot always be to the point. They would more likely be correct if they were based upon the absolute (p. 171 et seq.), instead of upon the actual sphygmogram, since we would then be comparing curves of the same frequency and gaining information in reference to the absolute volume of the diastolic fall.

In the absolute sphygmogram the sthenic fever would be characterized by a moderate, the asthenic fever by an excessive, diastolic fall of pressure. Typical examples of high tension pulse-curves are the arteriosclerotic pulse (Fig. 68), the nephritic pulse (Fig. 69), and the tense pulse in lead colic (Fig. 71).

Anacrotic elevations (p. 132) probably occur only with high blood-pressure. Fig. 71 shows anacrotism in some of the summits, and it is also suggested in the curve of Fig. 68. Rounded summits (Fig. 67) probably signify anacrotism consisting of several anacrotic elevations. The rigidity of the artery prevents it from being distinctly indicated. Similarly, rounded tops which slant off toward the descending limb should probably be imagined as confluent catacrotic elasticity elevations. Sometimes the rounded top is flattened like a plateau, but the significance is probably not changed. Such curves must not be confounded with those of the "negative sphygmogram." (See p. 134.)

SPECIFIC SPHYGMOGRAMS

When the sphygmograph was first employed, it was believed that pathognomonic pulse-curves would be found to characterize certain affections, especially cardiac cases. But such a belief has not been justified. Not even the curve of aortic insufficiency can be considered specific of this disease, for in fever and in exophthalmic goiter, without any leak at the aortic valve, a very pronounced pulsus celer is often observed. The pulse-curve of mitral lesions is less suggestive or certain, although in some instances it is of decided assistance in the diagnosis. A serious error was formerly made in the attempt to find characteristic signs in the curve during the time of disturbed compensation. This is evidently the least favorable time, because if compensation be affected to any extent, the pulse will always be small, weak, and of low tension; and such a condition might be due to the valve lesion alone, without any disturbance of compensation. v. Noorden[1] has par-

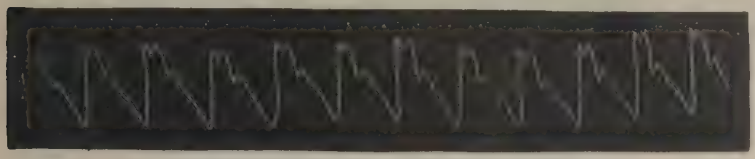


Fig. 72.—Tense pulse in compensated mitral stenosis (v. Noorden).

ticularly emphasized the necessity of utilizing well-compensated cases in order to obtain characteristic curves, and believes that compensated mitral stenosis exhibits a high-tension pulse, whereas compensated mitral insufficiency exhibits a low-tension pulse (Figs. 72 and 73).

v. Noorden accounts for this phenomenon by assuming that in mitral stenosis an increased arterial tone aids in maintaining the compensation. The arterial system is thus sufficiently filled and the pressure preserved despite the small systole. On the contrary, in mitral insufficiency the compensation is favored by vasomotor relaxation of the vessels, which diminishes the resistance in the arterial system. In this way a much larger proportion of the left ventricular contents can be utilized by the circulation, and a correspondingly smaller portion returns into the left auricle. These peculiarities are, the writer believes, more simply explained

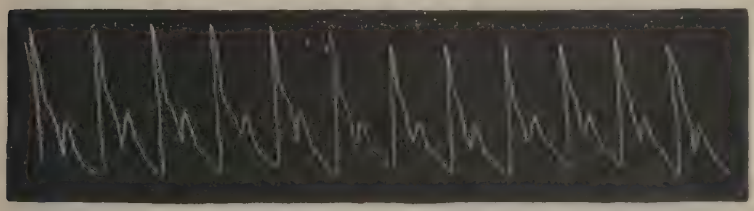


Fig. 73.—Lack of tension of the pulse in compensated mitral insufficiency (v. Noorden).

as follows: In mitral stenosis there is no reason for any diminution of the arterial pressure; whereas in pronounced mitral insufficiency a high arterial pressure cannot possibly occur because of the regurgitation of the blood into the left auricle. An approximately normal circulation in such a marked degree of mitral insufficiency, in spite of the low arterial pressure, is an indication that the vasomotor tone of the general circulation is lowered, a fact which has a compensatory significance, and to this extent v. Noorden is correct.

A FEW PRACTICAL EXAMPLES TO ILLUSTRATE THE APPLICATION OF THE SPHYGMOGRAPH

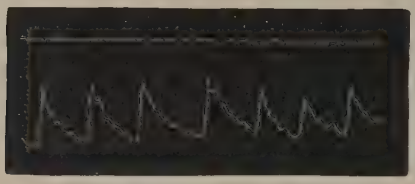
The deductions which may be made from the sphygmogram as to the condition of the circulation are well illustrated in Fig. 75, *a* and *b*, and Fig. 76, *a* and *b*. They

[1] Charité-Annalen, 15 Jahrgang.

represent tracings taken—(*a*) from a case of disturbed compensation and (*b*) from the same case after compensation has been reestablished by the employment of digitalis.

The comparison of curves in Fig. 75, *a*, and Fig. 77 is very interesting from a diagnostic standpoint. Both curves show an irregular pulse, but with these differences: The curve in Fig. 77 in general, and the small interposed beats, represent a

a



b

Fig. 74.—Sphygmogram from a patient with mitral insufficiency, to demonstrate the action of digitalis: *a*, Before the administration of digitalis—circulation decidedly affected, radial pulse 128, cardiac beats 172; *b*, after the employment of digitalis—circulation practically normal.

pulse of high tension, whereas the pointed single elevations of the curve in Fig. 75, *a*, point in general to a low degree of tension. The arterial pressure sinks quickly, especially in the little beats; this is evident from the dicrotism and from the depression of the base of the curve. The latter fact alone points to an insufficient systole as compared with the curve in Fig. 77, where the cardiac apparatus is evidently sufficient.

a

b

Fig. 75.—Sphygmogram from a patient with emphysema and cardiac dilatation, to demonstrate the action of digitalis: *a*, Before the administration of digitalis—circulation decidedly affected, pulse about 100; *b*, after 2 gm. of digitalis—circulation normal, pulse 70.

The type of irregularity illustrates another difference between the two curves. In Fig. 75, *a*, the size of the individual pulse-wave certainly in some places seems to be independent of the size of the preceding interval, whereas in Fig. 77 the size of the individual beat is directly proportional to the duration of the preceding interval. The first type of irregularity, according to the author's experience, always points to cardiac insufficiency, for when the pulse is smaller after a long pause than after

a short one (whether it be a normal systole or an extrasystole), this can be due only to an incomplete systole, and the condition can be helped by employing digitalis. This drug will improve the flow of blood through the cardiac muscle itself, and so help the disturbed innervation which is the cause of the arrhythmia.

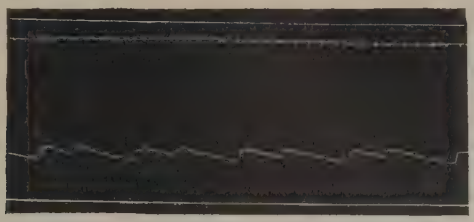


Fig. 76.—Pulsus bigeminus from extrasystoles, with compensatory pause, in a case of chronic pericarditis before the intravenous injection of 0.0003 digalen (Jaquet's sphygmograph, new model). This phenomenon was present for days.

The irregularity represented in Fig. 77 is quite different. Here the difference in volume of the beats is a direct sequence of the irregularity. Because the left

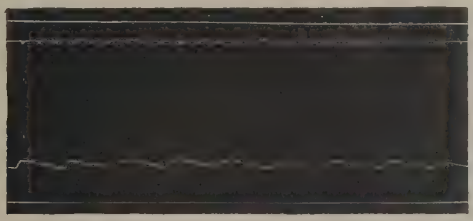


Fig. 77.—The pulse of the same patient, five minutes after the intravenous injection of digalen. The bigeminus has disappeared. Upon the other hand, however, it is well known that bigeminus not infrequently follows the administration of digitalis.

ventricular diastolic filling is brief, the succeeding pulse must be smaller, even if the cardiac power be entirely sufficient. This type of irregularity, therefore, does

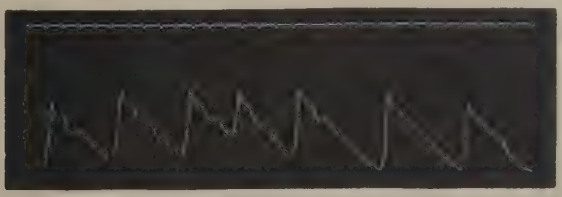


Fig. 78.—Arrhythmic sphygmogram in cardiac sufficiency.

not point to cardiac insufficiency, and so in itself presents no indication for the use of digitalis. The size and the high tension of the individual pulse-wave evident in Fig. 77 would be another reason for the uselessness of digitalis in this case.

THE EMPLOYMENT OF COMPARATIVE SPHYGMOGRAPHY IN THE DIAGNOSIS OF ANEURYSMS AND NARROWINGS OF THE MAIN ARTERIES GIVEN OFF BY THE AORTA

Marey[1] and Francois Franck[2] have made simultaneous records from vessels proximal and distal to an aortic aneurysm (p. 108), and found that the pulse-wave

[1] La Circulation du sang, 1881.

[2] Journal d'anatomie et de physiologie, 1878, vol. xiv.

in the distal vessel was delayed as compared with the pulse-wave in the proximal one. They also found that the delay was manifested both in the beginning of the ascent and, to a still more marked degree, in the apex of the curve. v. Ziemssen[1] and Mackenzie,[2] however, recognized only the delay in the apex of the curve, but none in the beginning of the ascending limb. Even to-day this question remains undecided, since the examinations have not always been made by methods free from objections. From what has previously been said in general, in reference to pulsus celer and pulsus tardus, it follows that a retardation of the apex of the curve must not be assumed from the general form of the ordinary sphygmogram (from the steepness of the ascending limb), but only from the absolute sphygmogram, or at least from a comparison of the duration of the ascent. Even a diminution in the size of the pulse-wave may simulate a pulsus tardus in the ordinary sphygmogram, just as the palpating finger may recognize both the delayed ascent and the delayed apex. The same statements are true of the retardation of the apex of the wave in an artery which is stenosed at its origin, such as is frequently the case with an artery coming off from an aneurysm by means of a distorted, slit-like opening. It is said that retardation of the apex occurs under these conditions, but such observations must be confirmed by measurement. Upon the other hand, both von Ziemssen and Mackenzie state that the beginning of the ascent occurs no later in a stenosed than in a corresponding normal artery.

Such simultaneous records may be taken by means of the instruments described upon p. 126 et seq. If the simplified Jaquet's sphygmocardiograph (p. 128) be employed, one artery is allowed to trace directly by means of the spring-sphygmograph, while the other traces upon the same strip of paper by means of pneumatic conduction. If we wish to compare two arteries, *e. g.*, the carotids, the curves of which can be comfortably taken only by pneumatic conduction, each carotid is in turn allowed to record itself in this way upon the same strip of paper which receives the direct synchronous tracing of the radial artery of the same side. The time relations of the two carotid curves may then be determined by comparison with the radial curves, which thus serve as a time-abscissa, Mackenzie's polygraph (p. 128) may also be advantageously employed for such records. With the exception of the radial artery, simple glass funnels or small metal beakers, such as those used by Mackenzie in his polygraph, may be utilized as receivers for the pneumatic registration (p. 128). If we wish to compare the two radial pulses and have no appropriate receptive appliance for the radial artery, we may take a direct tracing of each radial in turn, and upon the same strip of paper a synchronous pneumatic record from the carotid. This curve is easily obtained from the carotid without any special receiving appliance by means of a small funnel held by the hand. The carotid curve thus serves as a third factor in the comparison.

It should finally be stated that if it be desired to determine only the relation in time of the apex of the curve to the beginning of the ascent, this may be accomplished by taking two consecutive sphygmograms of the ordinary variety by means of the Jaquet sphygmograph, and then comparing them by means of the time markings.

THE MODERN ANALYSIS OF THE IRREGULAR PULSE

Introductory Note.—This chapter will consider chiefly the disturbances of the regularity of the pulse sequence as observed in the peripheral arteries, *i. e.*, pulse arrhythmia in the restricted sense of the word. It will also treat of the anomalies which sometimes occur, either with or without these arrhythmias, and which depend upon disturbances of the harmonic and physiologic coördination of the individual portions of the heart. It will finally take up the disturbances of the strength or volume of the arterial pulse as they occur from beat to beat, *i. e.*, the disturbances of the consecutive contractions of the heart, since all these disturbances have many points in common.

To understand what follows, we must take for granted Engelmann's supposition that the physiologic rhythmic stimulation for cardiac activity proceeds from the opening of the great veins into the heart to the auricle and the ventricle. The normal heart action is the physiologic response of the heart muscle to these physiologic rhythmic stimulations. In addition we must accept as proved (again according to Engelmann's experiments) that there must be differentiated as special properties of the heart-muscle fibers a power to produce stimulation, an irritability or stimulability, a power of conducting stimulation, and a capacity for contraction. These

[1] Arch. f. klin. Med., 1890, vol. xlvi.
[2] The Study of the Pulse, 1902.

peculiarities, Engelmann maintains, are inherent in the muscle-fibers themselves, but may be altered positively or negatively by many influences, which proceed partly from the nervous system. Engelmann differentiates *positive* or *negative chronotropic* influences, by which the number of the physiologic automatic stimulations is increased or diminished in the unit of time; *positive* or *negative bathmotropic influences*, which increase or diminish the irritability or stimulability; *positive* or *negative dromotropic* influences, which increase or diminish the conduction power of the heart-muscle fibers; and, finally, *positive and negative inotropic* influences, which affect the contracting power of the heart-muscle fibers.

Many regard the so-called "myogenic theory" of the cardiac activity as an integral portion of this teaching, according to which the cardinal characteristics described by Engelmann are peculiar to the muscular fibers themselves without the intervention of the neurocardium. This, however, does not seem justifiable, since these characteristics could still exist even if it were finally shown that all of them except contractility, which is, of course, a property of muscular tissue, are located in the neurocardium. The question is rather whether these characteristics are to be so sharply differentiated from one another as independent qualities, or whether they increase and diminish in harmony, and are consequently to be regarded as the expression of the general irritability of the myocardium or neurocardium.

In a great number of cases an exact analysis of the irregular pulse is possible only when all our methods of diagnosis are employed. The most important of these methods is sphygmography, which records the pulse in series of some length, and makes it accessible to exact measurement according to time and dimensions. For this purpose, the only sphygmographs to be employed are those, like Jaquet's or Dudgeon's, which record a long series of waves. The measurements are made along the abscissa, which furnish conclusions in reference to rhythm and of the height of the curve, which in this case gives us an accurate basis for comparing the volume and strength of the individual waves, because it refers to the same tracing. For the interpretation of the phenomena of the irregular pulse, however, we must also study the action of the heart as well as the pulsations of the radial artery. This may be done by palpation of the cardiac impulse, by auscultation, by inspection of the venous pulse, and, still more accurately, by a graphic record of the cardiac impulse taken synchronously with the arterial or with the venous pulse. Recently the synchronous sphygmographic records of the radial and of the venous pulse have furnished the most important and otherwise unobtainable conclusions as to the character of certain arrhythmias, since the venous pulse gives information in reference to the action of the right auricle and sometimes also to that of the right ventricle. The study of the venous pulse is consequently a prerequisite for the proper understanding of the following (p. 192 et seq.). A marked advance has been made by the instruments described on p. 120 et seq., particularly by the simplified Jaquet sphygmocardiograph and Mackenzie's polygraph, by means of which any practitioner may obtain the necessary simultaneous records of the various phenomena. Although but two different records may be made simultaneously with either of the above-mentioned instruments, we may take consecutively the carotid pulse and the radial pulse, the radial pulse and the cardiogram, and the radial pulse and the venous pulse, and then determine the relative times of all these phenomena, as is done by Mackenzie, by comparing them with the radial pulse, which thus serves as a basis of comparison. The following exposition of the analysis of the irregular pulse is consequently based upon a knowledge of the mutual relations of all these phenomena in reference to time. The credit for laying the foundation of the modern clinical analysis of pulse arrhythmias is due particularly to Wenkebach[1] and Mackenzie.[2]

For the proper understanding of what is to follow it is also necessary to have a clear conception of ineffectual systoles and of extrasystoles. By ineffectual (futile) systoles[3] we understand those which are not complete enough to produce a pulse-wave in the radial artery, and which may be recognized only by auscultation of the heart or by palpation or graphic records of the apex-beat. In such a case either only the first or two heart tones are audible to auscultation. The cause of the

[1] Zeit. f. klin. Med., 1899, vol. xxxvi; 1899, vol. xxxvii; and 1900, vol. xxxix; also the monograph, Die Arrhythmie als Ausdruck bestimmter Functions-störungen des Herzens, Leipzig, 1903.

[2] The Study of the Pulse, 1902.

[3] Quincke and Hochhaus, Deut. Arch. f. klin. Med., 1894, vol. liii, p. 414; see also the section upon ineffectual (futile) heart contractions in the chapter, "Cardiac Impulse."

futility may be either that the particular systole is so premature that the ventricle has not had time to fill sufficiently, or that the contraction is not strong enough to produce a perceptible pulse-wave in the peripheral artery. By an *extrasystole*, however, we mean simply a premature systole, and it matters not whether the peripheral pulse is of approximately normal volume or whether, as is usually the case, the pulse-wave is more or less diminished in size or even entirely absent (futile extrasystole). From this it follows that a futile systole is not necessarily an extrasystole, although such is usually the case, and that, upon the other hand, an extrasystole may be futile, but is not so of necessity. This terminologic consideration is of still greater necessity for the proper understanding of what is to follow, since a certain confusion upon this point exists in the literature. The cause of the dwarfing of the pulse-wave of extrasystole is a double one. It is usually due to the fact that the systole is so premature that the ventricle has not become sufficiently filled during the diastole to make possible a normal beat. In addition to this, however, an extrasystole may produce a diminished pulse-wave, because the heart has not had sufficient time to recover itself and consequently suffers in its contractility. Extrasystoles may occur singly in a pulse-tracing or in series of varying length. Single interpolated extrasystoles, if at all recognizable in the arterial pulse, manifest themselves as the pulsus bigeminus (Fig. 60, p. 138), *i. e.*, they form together with the preceding normal pulse a twin group which is separated from the following pulse by a longer pause, *i. e.*, by a longer depression of the pulse-wave. This pause may vary. It may be of the same duration as that of the normal pause, and in this case we speak of a shortened bigeminus, since the period of the pulsus bigeminus, taken as a whole (counting together the two pulses making up the bigeminus), is of shorter duration than the sum of two normal pulses. (See Fig. 79 from Mackenzie.)

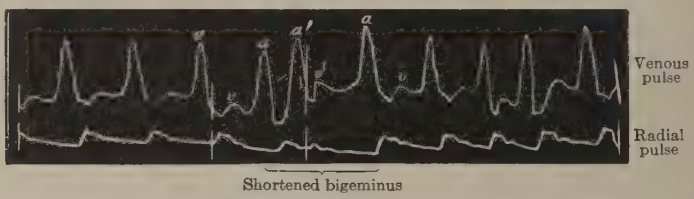


Fig. 79.—Shortened bigeminus. Auricular extrasystole, according to Mackenzie (*loc. cit.*, Fig. 266, p. 263), with shortened bigeminus. The extrasystole in the radial corresponds to a premature auricular wave *aa*. *a*, Auricular wave; *v*, so-called ventricular wave. (See p. 196.)

Upon the other hand, the pause following the extrasystole may be longer than a normal one—so long, in fact, that the following pulse occurs at just the same place it would have done had there been a normal instead of an extrasystole (Figs. 81 and 82). This lengthened pause is usually designated as a compensatory pause, since it compensates for the early extrasystole. In this case we speak of an unshortened bigeminus, since the duration of two systoles as a whole is not influenced by the premature systole. Between these two types of extrasystole there are transition forms which may be designated as instances of an incomplete compensatory pause or of an incompletely shortened bigeminus. The causes of these variations will be discussed with the different types of arrhythmia. It should also be noted that entire series of extrasystoles may be interpolated in the regular pulse sequence, so that we get a pulsus trigeminus, a pulsus quadrigeminus, or, when the number is still greater, what is known in general as a series of extrasystoles. In these cases the last extrasystole is separated from the following normal systole by either a normal or a compensatory (lengthened) pause.

A. Arrhythmias from Contractions Arising at an Abnormal Time (Arrhythmias from Extrasystoles)

(*a*) *Cases in which the auricles and ventricles*[1] *both take part in the irregularity dependent upon premature contraction, and in which the interval between the auricular and the ventricular contractions is consequently unchanged. Auricular extrasystoles.*

If a physiologic venous pulse be demonstrable, its rhythm coincides with that of the ventricle.

[1] The direct examination of the venous pulse gives us our knowledge in reference to the right auricle, and the contractions of the left ventricle may be studied in a similar manner.

In this class of arrhythmias Mackenzie differentiates those cases in which the pulse interval simply varies in an irregular manner about a certain average, and those in which a single premature contraction of the auricle and ventricle or a series of such contractions is interpolated in the regular pulse sequence. Mackenzie has observed instances of the first group, chiefly at the beginning of puberty, in individuals who are otherwise normal, and consequently designates them as infantile arrhythmias, or as the infantile type of arrhythmia. This type has also been observed by him in postfebrile bradycardia and during convalescence from cardiac disturbances in the adult. Although the accurate diagnosis of this type of arrhythmia must be based upon the persistence of the normal relationship between the venous and arterial pulses, the diagnosis is probably correct when the intervals vary irregularly, provided no pauses occur which correspond to double the normal pulse period, thus indicating futile extrasystoles absent in the radial, and, further, provided auscultation of the heart also reveals no futile systoles.

It must be admitted that the type designated by Mackenzie as infantile cannot be sharply differentiated from the other arrhythmias of this class (in which both auricle and ventricle exhibit arrhythmia in the same manner). It also seems more or less optional whether or not we should designate those systoles of the infantile arrhythmia which are preceded by shorter pauses as less premature extrasystoles, especially because here also they regularly seem somewhat diminished, as is the case with all extrasystoles. There is perhaps rather a graded difference between them and cases of this same group, in which the systoles are so premature that they induce an omission of the pulse or else produce markedly deformed pulse-curves at the radial artery, which are unmistakable extrasystoles.

An example of this latter type is seen in Fig. 79 from Mackenzie.

Since the right auricle takes part in all these cases in the same manner, we can characterize this group "*Aa*" as *auricular extrasystoles, i. e.*, extrasystoles which

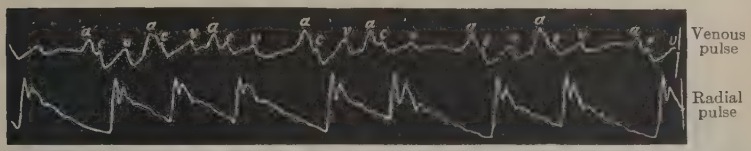


Fig. 80.—The infantile type of arrhythmia, according to Mackenzie (*loc. cit.*, Fig. 262, p. 261). The auricular venous pulse takes part in the disturbance. The lengthened pause gives no evidence of a contraction of any kind. *a*, Auricular wave; *v*, the so-called ventricular wave (p. 196); *c*, the carotid peak (p. 197).

originate in the auricle, from which the contraction is transmitted to the ventricle in the usual manner. A characteristic of this form of extrasystole is that the subsequent diastole is not necessarily materially lengthened. This is evidently due to the fact that in these cases the extrasystole acts exactly like a normal systole, so that after a diastole of normal duration the conditions producing the contraction repeat themselves. Such an instance is depicted in Fig. 79, where the sum of the duration of the preceding pulse and of the premature pulse is shorter than the duration of two normal pulses, and a so-called shortened bigeminus is produced. This condition is in contrast to the cases about to be described (see *Ab*), in which the extrasystoles proceed from the ventricle. It must, nevertheless, be noted that even with auricular extrasystoles, provided they are very large and not markedly premature, the diastole of the extrasystole may be longer than the normal diastole, and that a "compensatory pause" may consequently be present. As a result, the sum of the duration of the normal and of the premature pulses may equal the duration of two regular pulses (unshortened bigeminus), as is the case with ventricular extrasystoles (see below). This is an indication that the contraction stimulus following the extrasystole does not occur until the moment when it would have occurred without the extrasystole. Such an example is furnished in Fig. 81. Between these two types of auricular extrasystoles there are also transition forms, since sometimes the diastole of the extrasystole seems longer than normal, and yet not so long that the subsequent pulse and the extrasystole together are of longer duration than two regular pulses (incomplete compensatory pause). These differences possibly depend upon variable locations of the extra stimulus in the auricle. We might assume that when the extra stimulus is located at the site of the physiologic stimulus, the interval following the extrasystole equals the normal interval, because after this period of time the

normal amount of stimulus has collected; but when the extra stimulus is located in some other portion of the auricle, the site of the physiologic stimulus is rendered incapable of producing a stimulus for a longer or shorter period of time on account of the extra discharge which is conducted back there from the abnormal site. For the activity of the stimulus, as is well known, destroys the quantity of the stimulus.

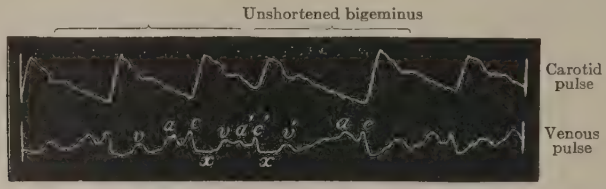


Fig. 81.—Auricular extrasystoles: a', Premature auricular contraction; v', premature ventricular contraction; c, premature carotid wave. The entire duration of the radial bigeminus corresponds to the duration of two regular beats. This is in contrast to Fig. 79, a, auricular wave; a', auricular extra wave; c, carotid peak (p. 197); c', carotid extra peak; and v', so-called ventricular waves (according to Mackenzie, *loc. cit.*, Fig. 286, p. 275) (p. 196).

From what has been said upon the subject it follows that auricular extrasystoles may be diagnosed from the artery only when the pause of the extrasystole is of normal length. When the pause of the extrasystole is lengthened, a simultaneous graphic record of the venous pulse is the only means by which we can determine whether the extrasystole is auricular or ventricular. It should be further noted that both auricular and ventricular extrasystoles may repeat themselves any number of times.

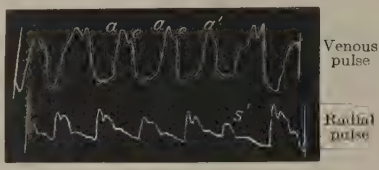


Fig. 82.—Ventricular extrasystole. The venous pulse proceeds regularly, while the radial pulse exhibits a premature beat (s') (according to Mackenzie, *loc. cit.*, Fig. 276, p. 270) (designations as in Fig. 81).

Under these circumstances, the characteristic features of the pause can be recognized only in the last extrasystole.

(*b*) *Cases in which the ventricle*[1] *alone takes part in the irregularity* (*ventricular extrasystoles, the pulsus intermittens*).

Ventricular extrasystoles are observed in the most diverse cardiac affections, and sometimes even in apparently healthy individuals. This very frequent occur-

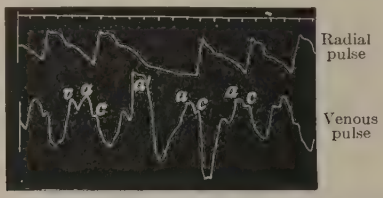


Fig. 83.—Futile extrasystole with a regular venous pulse. Ventricular bigeminus, unshortened bigeminus (according to Mackenzie, *loc. cit.*, Fig. 275, p. 269) (designations as in Fig. 81).

rence is illustrated in Fig. 82, the venous curve showing that the right auricle beats in a perfectly regular sequence, while in the radial curve a systole, s', is somewhat premature and consequently dwarfed. (See p. 154.)

From measurements of the intervals of the radial curve it will be seen that the bigeminus produced by the extrasystole, s', has exactly the same duration as two

[1] The left ventricle alone is accessible to examination.

normal pulses. The bigeminus is consequently unshortened, since the premature systole is equalized by a compensatory pause. In Fig. 83 a similar condition obtains, but with the difference that the extrasystole, which in this case was demonstrable only by auscultation of the heart or by a graphic record of the apex, does not appear at all in the radial curve, or rather is represented by an intermission of the pulse, while the auricular venous pulse proceeds in a perfectly regular manner. The regular series of the auricular venous pulses shows that the extrasystoles in this case must be ventricular. The reason why a compensatory pause is present is as follows: In a ventricular extrasystole the following normal contraction stimulus, which manifests itself in a contraction of the auricle at the normal time, reaches the ventricle at a moment when the ventricle has been left by the extrasystole in a so-called refractory phase, *i. e.*, incapable of contraction. A pulse is consequently not produced in the artery until the following normal ventricular systole. We have also just learned that the auricle may act in a similar manner in auricular extrasystole, probably when the extra stimulus acts upon some site other than that of the physiologic site for the origin of the stimulus. It consequently follows that the diagnosis of the ventricular origin of the extrasystole can be made certain only by the simultaneous record of the venous pulse. It should also be noted that the subsequent physiologic stimulus coming from the auricle may reach the ventricle when it is no longer in the refractory phase. In this case the extrasystole appears in the sphygmogram as an interpolated supernumerary pulse (pulsus intercidens, see p. 138), which falls between two pulses without increasing the interval between them.

B. Irregularities of Cardiac Action from Disturbance of Conductivity in the Heart

(*a*) *Arrhythmias from regular intermissions as a result of diminished conductivity within the heart. Pulse groups and ventricular bradycardias from disturbed conductivity. Partial or periodic heart-block.*

Fig. 84 represents a type of irregularity of the pulse which is characterized by regular intermissions occurring after a definite number of pulses. Wenkebach regards such occurrences as the result of a diminution of conductivity in the heart. To understand Wenkebach's explanation a few words are necessary. Engelmann

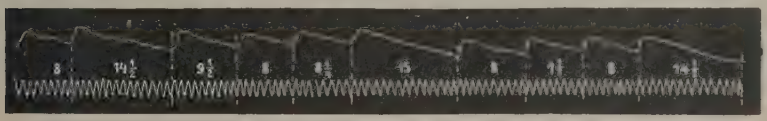


Fig. 84.—Regular intermitting pulse with groups of four pulses (after Wenkebach).

represented the amount of the conduction power within a certain section of the heart as Δ. The conduction power in the venous sinus is represented as $\Delta\ s$, that in the auricle as $\Delta\ a$, and that in the ventricle as $\Delta\ v$. $\Delta\ a\ v$ would then represent the power of conduction between the auricle and ventricle, etc. The time in which the contraction stimulus travels from one place to another depends upon the conduction power. The interval *As–Vs* (between the systole of the auricle and that of the ventricle) is of especial interest. During systole, not only the stimulability, but also the power of conduction Δ is diminished and this forms the basis of the so-called refractory phase. During the diastole both the stimulability and the power of conduction are gradually recuperated. With this explanation it is comprehensible that if the power of conduction, *e. g.*, at the boundary between the auricle and ventricle, be injured it may, after several heart-beats, become so much depressed that finally the stimulus no longer reaches the ventricular musculature in sufficient force to produce a contraction; but that after such a rest, in a certain way forced upon the ventricle, new beats will reappear. Given a certain degree of conduction weakness, this process may be repeated in such a way that one ventricular contraction will regularly be lost after a certain number of heart-beats, and so groups of regular pulses will be interrupted by an intermission. Such groups have for a long time been recognized in physiologic experiments, and called Lucian's periods. If we examine the sphygmogram in patients with such a regularly intermitting pulse more exactly, we find that the intervals between the pulse-beats within a group vary quite decidedly from each other; and that in each group this variation is repeated in a perfectly typical fashion. (See Fig. 84.) From a more accurate analysis of these variations in the intervals of the pulse within a group,

Wenkebach now shows that the regular loss of the pulse (which we are discussing) depends upon a negative dromotropic influence (see p. 153), *i. e.*, upon a disturbance of the conduction power. After the establishment of the pulse the first interval within a group is the largest, and the following intervals are decidedly smaller; but for the most part they again increase somewhat in size, up to a new intermission. This is explained by assuming from what follows (and, moreover, it has been experimentally proved by Engelmann) that the conduction power Δ is injured most by the first contraction after a pause, and is less markedly affected by the following contractions. The annexed diagram (Fig. 85), copied from Wenkebach, illustrates the relations very clearly.

The diagram is based upon the above assumption: that Δ is diminished by cardiac activity itself (by fatigue). The horizontal lines in the figure are to be considered as time abscissæ. The rhythmic physiologic stimulations which arise at the venous orifice are marked at regular intervals upon the time abscissa ϱ, 20 units apart. The uninterrupted lines drawn obliquely downward to the right are the graphic representations of the course of the stimulation from the venous orifices to the auricle and ventricle. The part of the figure included in the brace A represents the area of the auricle, that included within the brace V the area of the ventricle. The points of intersection of the oblique and horizontal lines represent the moments of time at which the physiologic stimulation, passing from the root of the heart to its apex, first, crosses the auricular border; second, stimulates the ventricular contraction. Wenkebach's own words furnish the best explanation of the rest of the diagram: "The rate of the stimulus contraction at the heart root

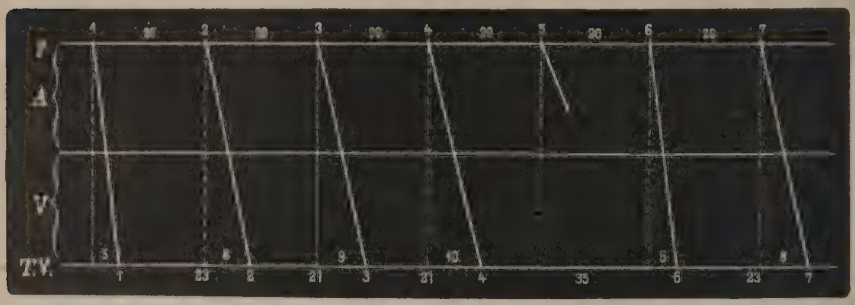


Fig. 85. Diagram to represent a regularly intermittent pulse, caused by disturbance of the conductivity of the heart muscle: one pulse is lost after every four (after Wenkebach).

$T\varrho = 20$; and the interval ϱ to Vs, that is the time between the stimulus ϱ and the ventricular systole Vs, in a favorable case (after a pause) = 5; but in an extreme case, where the stimulus is still transmitted just vigorously enough to produce a ventricular contraction = 10. During the contractions the interval ϱ to Vs is prolonged from 5 to 10. Following the experiment, we may assume that after the first systole of the group ϱ to Vs is increased 3; after the following systoles, ϱ to Vs is increased 1 each time.

"Should Δ in each contraction remain equal, as is normally the case, the tempo of the ventricular systole TVs would always equal ϱ, even if Δ be very slight. A diminution of Δ would occasion the proportionate increase of TVs. But since each systole has another influence upon Δ, the case will be quite different; and in the instance given here, the first interval (represented in the figure) of ventricular systole, $T_1Vs = 23$, being increased by 3, on account of the increase of the interval ϱ to Vs from 5 to 8. The following intervals of the ventricular systole, T_2Vs and $T_3Vs = 21$, on account of a further increase by 1. Then, however, the limit is reached, and the fifth stimulation is either not transmitted at all or is no longer sufficiently transmitted. The ventricular contraction fails, and an intermission results. The interval ϱ to Vs in this pause returns to 5, and the duration of the intermission (T int.) amounts to 5 less than the double of $T\varrho$; that is, T int. $= 2T\varrho - 5 = 35$. The same process is repeated after the intermission. The tempo of the ventricular contraction then depends entirely upon the rapidity of diminution of Δ in regular rhythm of the contraction stimulation, and with it the increase of ϱ to Vs."[1]

[1] Zeit. f. klin. Med., vol. xxxvii, p. 482.

Wenkebach found that the time relations in the accompanying sphygmogram (Fig. 84) were in complete conformity with this diagram (Fig. 85), and with the explanation given for the intermission. We observe in Fig. 84 that the numbers representing the intervals confirm the view that the periods after the intervals are the longest, the following much shorter, and those still later somewhat longer again. Although it cannot be recognized in the figure, a gradual diminution in the power of conduction occurs toward the end of a group in the pulse-curve, observed as a diminished celerity in the ascending limb of the pulse-wave.

Wenkebach considers that the exact measuring of the pulse-curve shows the size of the interval of the automatic stimulus at the venous orifices $T\varphi$, as well as the amount of the diminution of conduction power in the course of a group. The original article should be consulted in this connection.

Gaskel and Engelmann have called attention to the practical point that vagus irritation diminishes the size of Δ. In this way they explain the grouping frequently occurring after vagus stimulation, as well as the appearance of regular intermissions (especially the bigeminal and trigeminal pulse) after employing digitalis, as this drug stimulates the vagus. At the same time if there be a regularly intermittent pulse, digitalis increases the disturbance of rhythm, because it diminishes Δ by vagus stimulation. This also explains how atropin improves certain regular intermissions, as this poison depresses the vagus tonus, and thereby improves the conduction power of the heart muscle.

Still other anomalies of rhythm may arise from more pronounced diminution of Δ. These are all characterized by a certain amount of regularity or even by perfectly regular repetition of the intermissions, *i. e.*, some grouping of the pulses. However, if a longer pulse-curve be taken, the regularity of the grouping need not be absolutely even, because during the observation varied influences may affect the power of conduction. Any degree of gradation may occur between the ordinary

Fig. 86.—So-called "regularly double intermitting pulse" (pulse-groups separated by two longer cardiac revolutions) (after Wenkebach).

regular pulse rhythm and the regular pulse with half-frequency (bradycardia) depending upon the amount of injury to the conduction power, *i. e.*, the negative dromotropic influence. Such transitional forms are composed of groups of 6 to 2 pulse strokes. The regular intermitting pulse in groups of 2 strokes is nothing but a special form of the pulsus bigeminus.[1] The real pulsus alternans (p. 162) does not belong here; but according to Wenkebach, to a disturbance, not of the rhythm, but of contractility. In another group of cases the diminished power of conduction is expressed by the appearance, after the intermission, of a single systole, then another intermission, and then a group of several pulse-beats. This Wenkebach has called the "regularly double intermitting pulse," a term, however, which might lead to misunderstanding. Figs. 86 and 88 illustrate and explain the type. Still another serious disturbance of Δ will produce regular group formations, in which the groups are separated by 3, 4, 5, or n cardiac revolutions prolonged through the loss of a systole. Finally, if $n = \infty$, regular bradycardia with half-frequency occurs, as then only the second stimulation is permanently active. (See Fig. 88, γ, according to Mackenzie.)

In all the cases thus far described the diminution in conduction power goes only so far as to occasion the loss of a systole more or less often, but we may conceive of a case in which two or even several systoles, one immediately after the other, are lost; then longer pauses (*i. e.*, still more pronounced bradycardia) would result.

In such bradycardias the frequency of the venous pulse may be a multiple of

[1] Wenkebach is justified in calling attention to the fact that the terms pulsus bigeminus and trigeminus had better be discarded, since he shows in his particularly instructive book (p. 171) that sphygmograms requiring these designations are brought about in a number of different ways—by extrasystoles, by disturbed conductive power, and by true arrhythmias—and that, consequently, they should not be classed under one common name.

that of the radial pulse, and if the development of the phenomena be followed clinically it will be noted that the original frequency of the arterial pulse will be reduced suddenly or by groups of $\frac{1}{2}$, $\frac{1}{3}$, or $\frac{1}{4}$, etc. (See Fig. 88, *x*, according to Mackenzie.)

Since Wenkebach has not recorded the venous pulse in his published cases he has failed to furnish accurate proof that the grouping and bradycardia in his cases had been produced according to his supposition. It has been justly pointed out that such pulse groups and bradycardias may be brought about by auricular or ventricular extrasystoles, which repeat themselves in definite sequence and lead to intermissions of the radial pulse. Upon the other hand, Wenkebach's conception of certain types of bradycardia, in which the groups consist of but a single pulse, has been confirmed by Mackenzie by means of simultaneous records of the venous

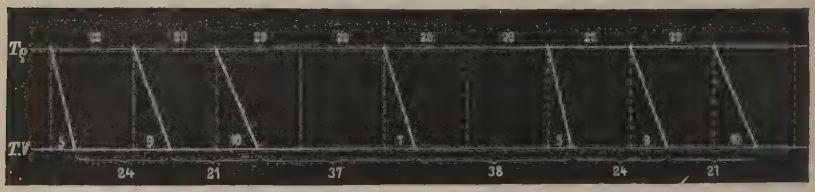


Fig. 87.—Diagram to explain Fig. 86 (after Wenkebach).

pulse (Fig. 88). Following the precedent of Gaskell and His, Jr.,[1] these cases are usually designated as heart-block, since the conduction of the stimulus from the auricle to the ventricle is blocked or interrupted for one or more systoles. In these cases, however, it would seem desirable to speak only of incomplete or periodic heart-block, because the blocking does not take place with every radial pulse, and because in the following section we will consider cases where the auricles and ventricles beat absolutely independently of one another. We should consequently reserve the expression heart-block, or, still better, complete heart-block, for this latter group. From the preceding observations the "ventricular" bradycardia associated with incomplete heart-block seems to be the usual cause of the slowing of the pulse in the so-called Stokes-Adams syndrome. The cause of the phenomenon, which consists in a disturbance of one of the fundamental qualities of the heart,

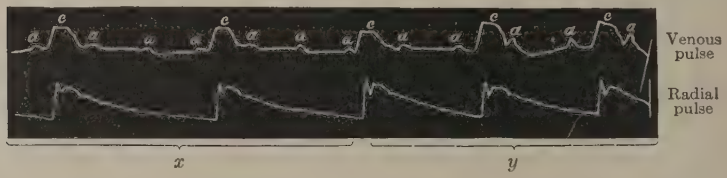


Fig. 88.—Bradycardia from the absence of ventricular pulses as a result of disturbed conduction. At *x*, two ventricular contractions are missing, at *y* one, while the continued presence of the regular stimulus is manifested in the curve of the venous pulse. A carotid peak (see p. 195) in the venous pulse is found only when there is a radial pulse (according to Mackenzie, *loc. cit.*, Fig. 292, p. 280).

explains the usually unfavorable prognosis of such a ventricular bradycardia. Other causes however, may probably be responsible for the Stokes-Adams syndrome. It might be, as in Fig. 89, for example, where there is no connection whatever between the ventricular activity and the auricular contractions, and the ventricle beats automatically in a regular and slowed rhythm, each contraction being, as it were, a ventricular extrasystole.

(*b*) *Complete dissociation of the ventricular rhythm from the rhythm of the auricles due to complete interruption of conduction. Complete heart-block with ventricular automatism. Horizontal dissociation of the heart.*

This occurrence is illustrated by Fig. 89, taken from Mackenzie. It is clear that these cases also can be recognized with certainty only by simultaneous records

[1] Deut. Arch. f. klin. Med., 1899, vol. lxiv, S. 316.

of the venous pulse. The nature of this complete heart-block is likewise doubtful. In the absence of a "ventricular wave" in the venous pulse (p. 197) Mackenzie sees the proof that in these cases also the right ventricle beats independently of the auricle. From the enlargement of the auricular wave of the venous pulse at the

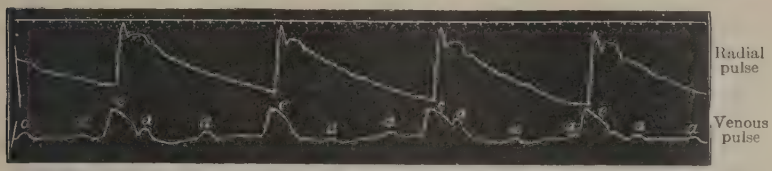


Fig. 89.—Complete dissociation of the ventricular rhythm from the rhythm of the auricles. Heart-block with automatism of the ventricles (according to Mackenzie, *loc. cit.*, Fig. 294, p. 282).

moment of its coincidence with a radial pulse he also concludes that the ventricles act synchronously—that there is simply a so-called horizontal dissociation of the auricles, upon the one hand, from the ventricles, upon the other.

C. Cases with Paralysis of the Auricles and Automatism of the Ventricles

These cases are particularly likely to occur in mitral lesions from the marked overdistention of the auricles. They are to be recognized by the complete absence of the auricular venous pulse, which is replaced by a ventricular venous pulse, either with or without tricuspid insufficiency. (See p. 197.) According to Mackenzie, the ventricular contractions appearing in the radial pulse are quite irregular in their character. Numerous extrasystoles are present in the radial pulse, which, from the nature of things, are frequently not followed by compensatory pauses, since the ventricular beat following the extrasystole is of autochthonous origin, or, in other words, all the ventricular contractions are extrasystoles. One series of extrasystoles may be recognized in the radial pulse, while the other series are futile and are apparent only from auscultation or from a record of the cardiac impulse. Futile extrasystoles in regular sequence may produce an apparent bradycardia in the radial pulse, the nature of which is revealed only by auscultation or by a cardiographic record.

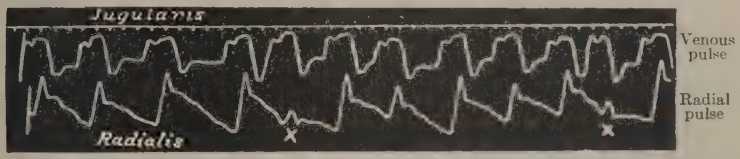


Fig. 90.—Ventricular venous pulse as a result of paralysis of the auricle. (See p. 197.) Complete coincidence of the venous and radial pulses. The rudimentary radial pulses correspond to venous pulses, since even a weak ventricular contraction has an obstructive effect upon the venous current (according to Mackenzie, *loc. cit.*, Fig. 296, p. 286).

Fig. 90 illustrates a complete auricular paralysis in which only ventricular pulses are present (see p. 197) with an arrhythmic radial pulse. From the coincidence of the ventricular venous pulses with the arterial pulses it is evident that both ventricles are working synchronously.

Mackenzie has demonstrated that at least certain forms of paroxysmal tachycardia are due to such instances of ventricular extrasystoles with paralyzed auricles, at least with a paralyzed right auricle, and he supposes that the paralysis of the auricles is not the cause of the entire disturbance, but that it is rather the consequence of an overdistention of the auricles resulting from the tachycardia.

D. Hemisystole (Vertical Dissociation of the Heart)[1]

By hemisystole is understood a peculiar type of cardiac activity in which one-half of the heart contracts more frequently than the other, or in which the ventricles contract independently of each other. The phenomenon might consequently be

[1] See also the section upon the Cardiac Impulse.

designated as a vertical dissociation of the cardiac activity. The diagnosis of hemisystole was formerly considered justified as soon as there were two venous pulses to one radial pulse, since the double venous pulsation was regarded as an indication that the right heart contracted twice as frequently as the left.

Since in partial and total heart-block we have become acquainted with examples of horizontal dissociation of the cardiac action in which the right auricle beats twice as often as the ventricles, it follows that the only justifiable conclusion to be drawn from such a doubling of the venous pulse is that the right auricle beats twice as frequently as the left ventricle. At all events, the occurrence of a hemisystole or a vertical dissociation of the cardiac action is quite a rare phenomenon. Such a possibility is not to be entirely excluded, however, since it has occurred repeatedly in animal experimentation, although usually not until just before death. Mackenzie gives two examples, which he is inclined to regard as instances of hemisystole; however, only one of his cases impresses the author as being possibly of this character, there being three ventricular venous pulses to two cardiac impulses (Mackenzie, *loc. cit.*, p. 277). A further objection which is still possible is that with the diminished contractibility, the contractions of the right ventricle can produce a ventricular pulse on account of the low intravenous pressure, while the corresponding radial pulse and even the apex-beat may be absent as a result of the cardiac weakness.

E. Disturbances of the Rhythm from Disturbances of the Contractility; Inotropic Arrhythmias; the Pulsus Alternans

The ventricular contraction may fail if the contractility of the heart muscle has been affected, even though the stimulus rhythm remains normal and the conduction power good. The resulting arrhythmia will be appreciable, both to palpation of the pulse and in the sphygmogram. In this case it depends merely upon negative inotropic influences. (See p. 153.) A grouping of more or less distinct regularity may occur from the summation of fatigue phenomena. The palpating fingers may obtain the impression of an arrhythmia even from a decided diminution of certain systoles. These arrhythmias, which the author would describe as "inotropic arrhythmias," can generally be diagnosed by the differences in the size of the pulses, although without any marked crowding of the periods. The pulses which fail, and to which no extrasystoles correspond, are, of course, excepted.

Pulsus alternans must be discussed here among the inotropic arrhythmias because it does not belong to the true arrhythmias and because it arises from a disturbance of contractility. A more careful examination and measurement of its pulse-curve shows that it presents a very characteristic though insignificant deviation of rhythm from the normal. It comprises a pulse series with large and small pulse-waves alternating regularly with one another at almost equal intervals. (See Fig. 62, p. 142.) Wenkebach[1] has analyzed this pulse most accurately, and decided that it depends upon a disturbance of the contractility for the following reasons: It certainly cannot depend upon a variation in the intensity of the contraction stimulus, because, as is well known, the heart always reacts maximally, even to a diminished stimulus, provided that the latter is sufficient to cause any contraction at all. For the same reason it cannot be due to a diminished power of conduction. It is incorrect to suppose that it could depend upon an extrasystole occurring practically half-way between two normal systoles; because, in the first place, it is quite exceptional for extrasystoles to persist regularly for so long a time, and especially because extrasystoles interposed almost in the place of the normal systoles would produce practically a normal pulse. Wenkebach's explanation is better. He considers that it depends upon a disturbance in the contractile power. After the stronger contraction, the contractile power is not sufficiently recuperated to respond with an equally vigorous systole to the next stimulus. After the weaker contraction, on the contrary, the heart muscle recuperates completely and the succeeding contraction is again more efficient. Regulated in this automatic fashion the pulsus alternans continues until the contraction ability becomes normal again. In conformity with the view that his cases of pulsus alternans depended upon a pure diminution of the contractility, Wenkebach adduces the earlier appearance (anticipation) of the smaller pulse, *i. e.*, the interval between greater and smaller pulse is shorter than that between smaller and greater pulse. In explanation he assumes that the stronger and weaker contractions differ not only in their strength, but also in the rapidity of their occurrence. B. F. Hoffmann,[2] in fact, did demonstrate that the contractions of the heart muscles

[1] Zeit. f. klin. Med., 1902, vol. xliv, parts 3, 4, p. 218.

[2] Pflüger's Archiv, 1901, vol. lxxxiv.

occur more rapidly in a hypodynamic condition (*i. e.*, with less contractile power) than with normal contractility. If we assume that the smaller beats of the pulsus alternans occur more rapidly than the larger, it follows that the beginning of the smaller pulse will anticipate in the radial curve, as contrasted with the beginning of the greater pulse, because it is more rapidly transmitted to the peripheral arteries.

Volhard has shown, however, that a pulse-curve possessing the characteristic described by Wenkebach, viz., the smaller arterial pulse anticipates, should not be called a true alternans, but rather a pseudoalternans. That is to say, it is not to be regarded as the result of a pure disturbance of contractility, but as a disturbance of rhythm from bigemina or from extrasystoles, and that the true alternans, on the contrary, is characterized by the fact that the smaller pulse in the artery is somewhat delayed. For a more minute description of this conception the reader is referred to Volhard's discussion in the Münch. med. Wochenschrift, 1905, No. 13, and only the important conclusions of this author will be given, in reference to the differential diagnosis between the true alternans and the pseudoalternans. These conclusions are:

1. There occurs in the human subject a true cardiac alternation; a rhythmic sequence of stronger and of weaker systoles of the auricles and of the ventricles.

2. A disturbance of rhythm is not manifest at the heart, but only in the pulse, where the smaller pulse-wave seems to be somewhat delayed.

3. This delay in the pulse is not due to impaired conductivity, but to a prolonged contraction time and to a slower transmission of the small wave in the artery.

The prolonged contraction time is caused by the more sluggish course of the smaller systole and by the greater resistance in the aorta at the time of the smaller systole.

4. If an extrasystole appear in a pulsus alternans, the alternation may become so accentuated that the second pulse intermits.

5. There is but a *single* form of the pulsus alternans, the one with the *delayed* smaller wave. If the smaller wave appear at the normal time or even somewhat before it, the pulse is a *pseudoalternans*, due to extrasystoles.[1]

6. In true alternans the delay of the smaller pulse destroys the equality and simulates a disturbance of rhythm; in pseudoalternans it destroys the disturbance of rhythm and simulates equality.

In view of Volhard's studies, a figure in the last edition must be regarded as a pseudoalternans, and has consequently been replaced by one of Volhard's curves (Fig. 62, p. 142), which, from the accompanying cardiogram, must be designated as a true alternans.

SPHYGMOMANOMETRY (TONOMETRY)

THE DETERMINATION OF THE ARTERIAL MAXIMUM PRESSURE (SYSTOLIC PRESSURE)

The sphygmograph furnishes only relative information of the height of the arterial pressure; hence von Basch[2] attempted to construct an instrument to measure the arterial pressure upon the living human body. He succeeded, approximately, with the sphygmomanometer. Potain has since modified von Basch's modernized instrument.

Von Basch attempted to copy the method of estimating pulse "tension" with the finger (p. 115) by measuring instrumentally the amount of pressure required to suppress the pulse-wave. Waldenburg, Talma, and Verdin had attempted to obliterate the pulse in the artery by compressing the artery by weights or springs. The size of the surface pressed upon was neglected in these experiments, so that their results are of no particular value. To obviate this difficulty, von Basch devised a so-called air pelotte, which he connected to a spring manometer by means of a rubber tube. The pelotte consisted of a short hollow metal cylinder, each end of which was capped with a thin rubber membrane. With this mechanism the size of the surface pressed upon makes no difference; the manometer reading will always be the same, for, according to hydrostatic laws, the amount of pressure indicated by the manometer is that exerted upon each point of the surface of the pelotte.

[1] If the difference in sizes of the pulse be very slight, the intervals even in true alternans may nevertheless be approximately equal, *i. e.*, the delay in the pulse may be inappreciable.

[2] Berlin. klin. Woch., 1887; Arch. de physiologie, 1889, Ser. 5, vol. i, p. 556, and vol. ii, p. 300.

Von Basch's Sphygmomanometer.—Fig. 91 represents a modified form of the instrument: *A*, the manometer; *B*, the pelotte; *C*, the connecting tube. By means of the cock, *D*, the entire system is filled with air under a low pressure,[1] so that the pelotte is but slightly tense, and the two closing members bulge a trifle.

The employment of this instrument is very simple. The course of the artery to be examined is first marked upon the skin; one of the bulging membranes of the pelotte is placed upon the artery, and the manometer is laid upon the bed at the side of the patient. The examiner then attempts to estimate the amount of pressure (read upon the manometer scale) necessary to obliterate the pulse peripheral to the pelotte. This he does by palpating with one finger, while with another he prevents any anastomotic pulse from entering the artery. This method will determine the arterial pressure. The result will perhaps be more accurate if the manometer be read at the moment when the pulse reappears after the pressure has been gradually diminished. The measurement is usually made upon the radial artery, although the temporal may also be employed. To utilize the results obtained the difference in level between the artery and the heart must be given. Since the arterial pressure varies with the position of the body, the attitude of the patient during the measurement (standing, lying, sittng) should also be stated. The method is, of course, entirely subjective, as its accuracy must depend upon the examiner's sense of touch. To obviate this difficulty, v. Basch has attempted to substitute the sense of sight. A rubber band is rather loosely placed over the radial artery, and a small pin stuck in it, so that the excursions of the pin are plainly visible. If the pin stop moving, the pulse is considered absent. According to the author's experience, this device is not always successful. In order to make the measurement more objective, the author prefers the combination of the Riva-Rocci method with the employment of the sphygmograph. (See p. 175.)

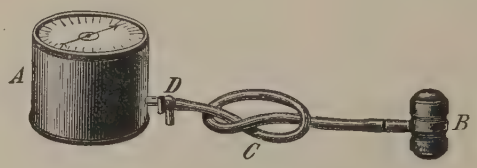


Fig. 91.—Von Basch's sphygmomanometer.

Two factors combine to prevent this method from measuring the true arterial pressure accurately. In the first place, the wall of even an empty artery remains open, so that a certain, though small, amount of the pressure exerted represents that employed to compress the arterial tube; and, in the second place, the tissues covering the artery must interfere to a slight extent with the accurate application of the pelotte, so that the instrument must register a somewhat higher pressure than actually exists.

Von Basch's experiments, however, show that both these factors combined cannot cause a deviation of the real values from those recorded of more than about 10 to 15 mm. Tigerstedt[2] gave a very unfavorable opinion of the value of this method, because he found a much greater deviation. In the first three editions of this book the author shared his view, but feels obliged to withdraw his criticism since he has used the improved air pelotte, as illustrated in Fig. 91, together with his own manometer. As a matter of fact, the results given by the old pelotte were not very reliable, for reasons which cannot be here given in detail. The temporal artery is the most conveniently situated for this measurement; the radial next, since it is compressible against the lower end of the radius. In the former von Basch found that the normal pressure varied from 99 to 120 mm. Hg; in the latter, from 110 to 160. The author's own estimations at the radial, in healthy adults with the new pelotte (see below), have usually been about 150 mm. In a pathologic increase of pressure, values over 250 mm. may be obtained. Potain's investigations (*loc. cit.*) show that these figures correspond to the maximum pressure variations during a pulse-wave, *i. e.*, to the systolic pressure.

[1] Von Basch formerly filled the cylinder with water. Air was first employed by Potain, and has the advantage of doing away with hydrostatic pressure, and so enabling us to disregard the level of the manometer in reference to the pelotte.

[2] Lehrbuch der Physiologie des Kreislaufes, Leipzig, 1893.

Another reason to doubt the accuracy of this method is the following: since dynamic processes (that is, moving masses) are chiefly concerned, we must consider the vital power of the pulse-wave according to the laws of the hydraulic press. Now, it is well known that when a current is checked by some obstruction, its lateral pressure above the obstruction is far greater at the moment of checking than the lateral pressure of an unobstructed stream. This arises from the transformation of the pressure of velocity into lateral pressure. The hydraulic press or ram depends upon this principle. This is true not only of uniform currents, but also of the wave-like impacts of the arterial pulse. Consequently a large pulse-wave, even with low arterial pressure, will force its way through under the compressing pelotte, owing to the greater amount of "energy," while a smaller pulse-wave, even with higher arterial tension, will be completely obstructed, because the latter possesses less energy. Again, the portion of the wave which passes through under the pelotte will be felt longer if the pulse be large than if it be small and hard to feel, even though of high tension. In one of the author's works,[1] however, he has shown that the sources of error[2] of this method, connected with the energy or volume of the pulse-wave, are not sufficient to impair materially its value for the determination of the systolic or maximal blood-pressure. Potain, as mentioned above, has also found that the method in question indicates the so-called maximum, *i. e.*, the cardiac systolic pressure. This is in accord with the view just expressed, that the energy or volume of the pulse-wave has no essential influence upon the disappearance of the peripheral pulse.

From the discussion upon the determination of the minimum pressure by means of the Riva-Rocci method (see p. 175) it will be seen that von Basch's instrument may be likewise employed for the determination of the minimum blood-pressure if we determine the pressure of the pelotte under which the peripheral pulse commences to become smaller. This procedure, however, is of only approximate value, and considerable experience is requisite to determine this exact moment with any degree of certainty.

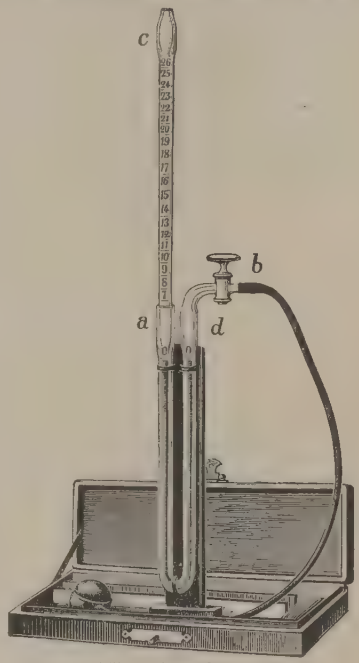


Fig. 92.—Sahli's pocket sphygmomanometer.

Sahli's Pocket Sphygmomanometer.—The author has made what he believes to be an improvement in von Basch's instrument by increasing the diameter of the air pelotte from scarcely 2 cm. to about 3 cm. This greatly aids us in securing pneumatic pressure upon the artery; while with the small pelotte of von Basch there is danger of compressing the vessel by the resistant portion of the caoutchouc near the rim of the pelotte or by the rim itself.

As it has also been the author's experience that the metal manometer of the shops is not very accurately graduated, and that, although it may be correct originally, the values of the scale gradually change, he has constructed a pocket mercury manometer, which may be easily transported, is absolutely correct, and has the additional advantage of being cheap.[3] This manometer may also be employed for any other manometric method, in the Riva-Rocci sphygmomanometer, for example. (See p. 166 et seq.) The instrument is illustrated in Fig. 59, and consists simply of a U-shaped manometer, one branch of which can be elongated by inserting a

[1] Ueber das absolute Sphygmogram u.s.w., Arch. f. klin. Med., 1904, vol. lxxxi.

[2] Although the author's statements refer to the Riva-Rocci method, they are equally true for the pelotte method, since there is no difference in principle between the two.

[3] The instrument is manufactured by the optician Büchi, in Bern.

glass tube, the connection being accurately ground. The caliber is sufficiently large to exclude the disturbing element of capillarity, and yet not large enough to require a great quantity of mercury. Owing to the accurate adaptation of the two tubes, it is unnecessary to use the greasy materials usually employed to secure the perfect adjustment of glass stop-cocks, and the mercury is consequently kept in much better condition. When the instrument is to be employed, the extension *a c* is inserted, and a pneumatic pelotte, such as that of von Basch's instrument (preferably the enlarged form, as described upon p. 164; see Fig. 91) is connected with *b* by a tube. The pressure exercised upon the artery by the pelotte is transmitted to the shorter arm of the manometer. The elongated arm is so divided that it gives the pressure directly in centimeters, every half-centimeter being marked as a unit. In such a manometer, as is well known, the pressure is obtained by multiplying the height of the ascending column by two, because the mercury falls exactly as far in one branch as it rises in the other. The manometer must be accurately filled with mercury to the zero mark. The ampulla *d* is constructed to prevent forcing the mercury out of the shorter branch by a sudden diminution of pressure, and the ampulla *c* acts in a similar manner if the pressure be suddenly increased by careless manipulation of the pelotte. The instrument may be packed for transportation by removing the extension tube *ac*, plugging the opening *a* with a tightly fitting cork, and closing the other end by turning the glass stop-cock. Rubber corks are not suitable because the formation of mercuric sulphid would dirty the glass tube. A convenient case carefully cush-

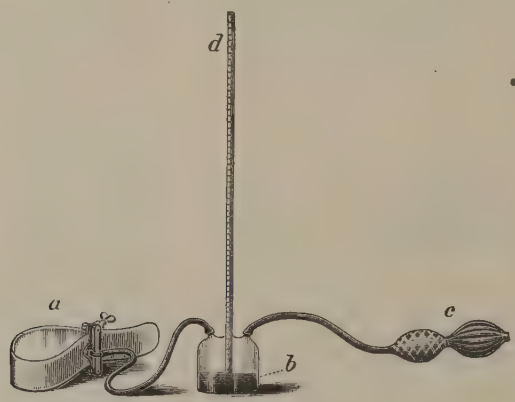


Fig. 93.—Sphygmomanometer (after Riva-Rocci).

ioned to prevent breaking is supplied and is made large enough to hold a pelotte as well. With such an instrument one determines values which are almost exactly in accord with those obtained with Riva-Rocci's instrument. In fact, the former values are even more reliable, because they are obtained from a superficial artery and so almost entirely uninfluenced by soft parts.

Since the mean blood-pressure is so important for diagnosis, as well as for determining the efficiency of certain therapeutic agents, it is very fortunate that so many physiologists have recently turned their attention toward devising some simple and accurate method of measuring it. Such methods have been described by Mosso, Hürthle, v. Frey, Riva-Rocci, and Gärtner.

The Riva-Rocci and the Gärtner instruments are the only ones which have proved to be practically valuable, and are, therefore, the only instruments described in this edition.

Riva-Rocci's Sphygmomanometer.[1]—Its principle is similar to that of von Basch's. It measures the amount of pressure necessary to obliterate the pulse peripheral to a point of constriction. A pneumatic pressure is used as in von Basch's instrument. The practically important modification consists in substituting for the pelotte used to press upon the artery a pneumatic cuff (*a*, Fig. 93), which encircles the upper

[1] Riva-Rocci, Un nuovo sfigmomanometro, Torino, 1896; Frascati e Comp. Technica della sfigmomanometria, Gaz. Med. di Torino, 1897, Nos. 9 and 10.

arm, and the cavity of which connects with a rubber bulb. Since the upper arm contains only a single bone, inflation of the cuff will interrupt all the arterial supply to the forearm in a perfectly equal way.

The cuff should be made of some firm mackintosh cloth, or, if of elastic rubber, it should be covered, at least on the outside, with some material which will not stretch. This is to prevent the loss of a part of the pressure from any eccentric inflation or distention of the wall. Fig. 93 represents the original form of the apparatus.

[In America, Cook rendered a great service by so modifying the Riva-Rocci apparatus as to make it inexpensive and portable,[1] thus securing for it a much more extended application. His instrument so closely resembles its original in the technic of its use that it needs no further description.—Ed.]

Fig. 92 represents a convenient modification of the instrument used by the author. The portable manometer (Fig. 94) is connected with the bulb and the cuff by a T tube. Büchi (Bern) supplies this apparatus; the cuffs were designed by the author. The cuffs come in two widths, 6 and 8 cm., and are closed by a clamp employing a lever instead of the rather clumsy screws of the original apparatus. Of late a simpler and cheaper model, something like the American one, has been used, in which the cuff is attached by a leather or canvas strap, passing around it and

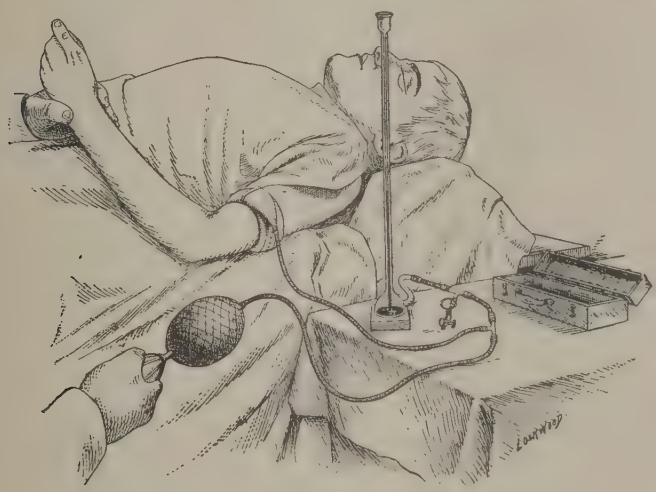


Fig. 94.—Riva-Rocci sphygmomanometer as modified by Cook.

fastened by a buckle. The broader cuffs are now preferred, not so much on account of v. Recklinghausen's criticism of the narrower one (see p. 168), as because, if the arm be very soft and fat, a high pressure will be apt to make the inner layer of the narrow cuffs bulge out to the side along the edge. The broad cuff may also be used to advantage in sphygmobolometry. (See p. 180.)

The patient's upper arm is inserted into the cuff (*a*). The latter is connected with a mercury manometer (*b*), or the author's portable manometer (Figs. 92 and 94), and through it with a double rubber bulb (*c*). By pumping at *c* the cuff can be made to encircle the upper arm snugly, but without much compression, and the amount of pressure employed can be read in millimeters of mercury upon the vertical tube of the manometer. This pressure is increased until the radial pulse disappears. The method was tested by Riva-Rocci on animals; and by Gumprecht,[2] on the human cadaver: and, according to them, if the muscles be well relaxed, the circumstance that the compression is applied through thick muscles does not invalidate the result. Fellner's and Rüdinger's[3] experiments on dogs were less favorable.

[1] H. W. Cook, Jour. Amer. Med. Assoc., 1903, vol. xl, p. 1199.
[2] Zeit. f. klin. Med., 1900, vol. xxxix, Parts 5 and 6.
[3] Ibid., vol. lvii, Parts 1 and 2, p. 125.

They showed that the maximum and minimum pressures obtained by the Riva-Rocci method differ from those measured directly by a manometer, sometimes by as much as 50 or 70 mm. Yet the difference between the maximum and the minimum pressure ("pulse pressure," height of the absolute sphygmogram) agrees with that obtained by a direct manometer.[1] The author believes that these experiments on dogs do not furnish satisfactory data for conclusions as to the value of the procedure with human subjects, as the shape of the dog's leg is probably a disturbing factor and so, too, very likely is the hairy surface.

The maximum or systolic pressure is given by the reading at the moment of the disappearance of the pulse, the same as with von Basch's instrument. (See p. 164.) Normal adults furnish with the Riva-Rocci apparatus a value of 140 to 150 mm. Hg[2]; and arteriosclerotics and nephritics up to 230 to 250 mm., or even higher. For control it is well to raise the pressure beyond the point at which the pulse cannot be felt, and then, when, as a result of the yielding of the rubber tubes[3] and connections, the pressure falls slowly, the point is noted at which the pulse begins to appear again. In this way the attention is not distracted by the need of pumping, and the method is still more objective and quite exact. The author has frequently attempted to supplant the palpation of the pulse by the objective method of sphygmography, making short curves at different pressures until the needle makes but a straight line. It has advantages in demonstrating to a clinic. One caution should be added. Pronounced congestion, pain, and even cutaneous hemorrhage may result from employing the instrument to measure very high pressure, *e. g.*, above 230 mm.

The author has found the results obtained by Riva-Rocci's instrument agree very closely with those obtained by von Basch's method as modified by him. (See p. 165.) Apparently the two procedures are equally accurate. (For the measurement of the minimum pressure with Riva-Rocci's instrument see the section on the absolute sphygmogram, p. 174.)

Led by v. Recklinghausen,[4] a number of writers have pointed out that the cuff of Riva-Rocci's original instrument is too narrow. They came to this conclusion from the fact that different values are obtained when a wider cuff is employed. It is clear that if the cuff be too narrow, the inflation produces a marked distortion, both of the cuff itself and of the surface of the arm, which endangers the transmission of the aërostatic pressure, since a certain fractional part of the manometric pressure is consumed in producing the aërostatic tension of the cuff and the tension of the tissues pressed upon. The cuff of the original Riva-Rocci instrument was 4.5 cm. in width. These authors now demand a cuff 32 cm. wide. This makes the instrument more clumsy. Additional errors also arise from the fact that such a broad cuff does not act upon an approximately cylindric surface, owing

[1] In opposition to this view, according to the author, is the statement of these investigators that the Strassburg blood-pressure quotient (ratio of the pulse pressure to the maximum pressure, see below) can be determined accurately by the Riva-Rocci method; although these figures must be decidedly influenced by the deviation of the maximum pressure.

[2] The blood-pressure in normal children has been carefully studied by Oppenheimer and Bauchwitz; see Arch. f. Kinderheilkunde, vol. xlii, p. 145. The following values were obtained by the author with Riva-Rocci's instrument, and are quoted here because the above-named investigators do not furnish exact normal figures derived from a large series of examinations:

Age.	Height.	Blood-pressure.
12 years	136 cm. (54 in.)	112 mm.
10 "	125 " (49 ")	110 "
4 "	100 " (40 ")	110 "
8 months	73 " (29 ")	96 "
8 weeks	61 " (24 ")	92 "
6 "	53 " (21 ")	90 "
6 "	51 " (20 ")	80 "
5 "	59 " (23 ")	84 "

[3] In case the apparatus is absolutely air-tight, a capillary escape tube may be inserted between the cuff and the bulb (see section on Sphygmobolometry, p. 181), and thus air be allowed to escape gradually by means of a glass stop-cock.

[4] Recklinghausen, Arch. f exp. Pathol. u. Pharm., 1901, vol. xlvi, parts 1 and 2; Hensen, Deut. Arch. f. klin. Med., 1900, vol. lxvii.

to the irregular contour of the arm. Martin[1] has found that a cuff 10 cm. in width suffices for all cases. In the author's opinion a great deal depends upon the material of which the cuff is made, upon the flexibility of its outer layer, and upon the manner in which it is applied.[2] The author has treated this subject more freely in his article on the absolute sphygmogram.[3] The very wide cuffs are particularly

Fig. 95.—The author's sphygmomanometer in use, according to Riva-Rocci's method.

useful in sphygmobolometry. If the cuff be emptied and applied accurately to the skin without the exercise of any pressure, cuffs only 5 to 6 cm. in width remain so

[1] Münch. med. Woch., 1903, No. 24, p. 1021.

[2] Neglect of these considerations may explain the great divergence of opinion regarding the value and practicability of the different widths.

[3] Arch. f. klin. Med., 1904, vol. lxxxi.

flat during inflation that the transmission of the pressure is complete and the results are as accurate as they can well be from the nature of the procedure. We should banish the illusion that this procedure equals the accuracy of manometry upon the exposed and divided artery.

[*Hill and Barnard's Sphygmometer.*[1]—This instrument appeared in England a little after Riva-Rocci's, and uses the same method of circular compression. It does not, however, measure the pressure required to obliterate the pulse (systolic or maximum pressure), but, like Mosso's, the point of maximum pulsation (diastolic or minimum pressure). This is accomplished by the employment of a delicate spring tambour, graduated in mm. Hg., as the manometer. Fig. 96 shows the apparatus. The cuff, a hollow bag, 4.5 cm. wide, with an outer leather armlet, is buckled around the arm, and connected with the manometer by a screw-joint. The pressure is then raised by means of the hand-pump until the needle shows diminishing excursions on the dial. Then, by unscrewing a valve in the stem of the pump, the pressure is allowed to fall gradually, while the needle is closely watched. Its oscillations increase for a time to a maximum, then, after remaining the same for a short time, rapidly decrease. The last point at which they remain maximal represents the minimum arterial pressure, as already described. Hill thought that the midpoint of maximum oscillation was equivalent to the mean arterial tension, but this has been proved inaccurate. The instrument is well constructed, light, and compact. It has two drawbacks. One is the narrowness of

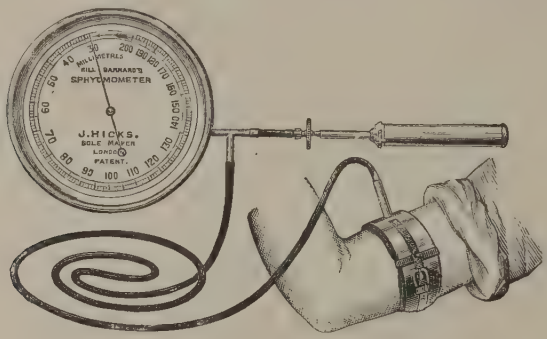


Fig. 96.—Hill and Barnard's sphygmometer.

the cuff. The other is, that so delicate a manometer needs constant standardizing by comparison with a mercury one, and soon becomes inaccurate.—Ed.]

Gärtner's tonometer[2] depends upon a similar principle. It estimates the pressure which is required to interrupt the peripheral circulation. Gärtner makes use of the color of the tip of the finger instead of feeling the pulse to determine the condition of the peripheral circulation. His instrument consists of a small pneumatic compression ring, whose cavity is connected with a mercury or spring manometer and with a rubber bulb. The pneumatic ring is constructed of a metal hoop 1 cm. high and 2½ cm. in diameter. A rubber membrane lines this hoop, and with the latter surrounds an air-space communicating with the manometer and bulb. The pneumatic ring is first slipped over the second phalanx of the little finger without pressure. The projecting end phalanx is then made bloodless by a rubber compressor like a glove-finger, or by a ring cut out of a rubber tubing, rolled upon the finger as far as the pneumatic ring. This compression is kept up until the pressure in the pneumatic ring has been raised by means of the bulb sufficiently to keep the blood from returning to the finger; then the compressor is removed. The finger-tip now appears bloodless. By gradually releasing the pressure from the rubber bulb the finger becomes colored again. As a matter of fact, the finger be-

[1] Hill, L.; Barnard, H., Brit. Med. Jour., 1897, vol. ii, p. 904. Made by J. Hicks, London; agents for the United States, Oelschlager Bros., 110 East 23d St., New York City.

[2] G. Gärtner, Ueber einen neuen Blutdruckmesser (Tonometer), Wien. med. Presse, 1899, No. 26. L. Schulmeister (Vienna) and F. Hugershoff (Leipzig) make the instrument.

comes deeply colored, and so facilitates the differentiation. This is because the veins will still be compressed at the moment the digital arteries open under the arterial blood-pressure. This pressure at which the blood again streams into the finger can be regarded as equivalent to the blood-pressure in the digital arteries. In cases where the capillaries of the finger-tip are much contracted, it may happen that the finger-tip will not be properly colored after the release of the pressure on the arteries. In such cases Gärtner accomplished his purpose by relaxing the tonus of the fine vessels by producing an artificial congestion from a pressure of 20 to 40 mm. Hg with the pneumatic ring for a half minute, and so paralyzing the vessels just before repeating the test. Gärtner assumes that the pressure in the small digital arteries differs but little from that in the radial. Of course, the measurement will be decidedly influenced by the height of the fingers, so that he recommends that the test be undertaken with the fingers at the height of the heart. The normal pressure values Gärtner has estimated vary between 90 and 105 mm. These are less than those obtained either by von Basch's or Riva-Rocci's method, a fact which militates against Gärtner's original assumption that the pressure at the finger-tips does not vary essentially from that in the radial artery. Another objection to the method is that the readings are decidedly influenced by the resistance of the tissues of the finger-tips. This resistance is very different in a laborer's hand and in a lady's hand. In the writer's opinion, these sources of error are so considerable that it discounts the value of the entire procedure, except in determining the variations of pressure in the same individual at different times. Certain technical modifications of this method[1] do not obviate this chief fault. It may be added that Gärtner's method of employing the sense of sight may also be used in connection with the Riva-Rocci instrument, by encircling the arm with an Esmarch bandage before the procedure.

Von Recklinghausen's Blood-pressure Apparatus.—This instrument has been used to a considerable extent recently. It is constructed according to the principles of Riva-Rocci's; and differs from the other clinical blood-pressure instruments chiefly in the construction of its manometer, which the inventor calls a *tonometer*. This, a metallic manometer, consists of a short, lightly curved bourdon tube, shallow oval in cross-section. The effect of changing pressure upon its inner wall alters its shape, and transfers its excursions to an indicator, which in turn registers the pressure values upon a dial. If, as in all metallic manometers, the zero point be dislocated, the indicator can be properly adjusted by means of a screw. This device, and a more careful construction, distinguish the instrument from the other ordinary metallic manometers (von Basch's and Potain's, for example) to its own advantage. The latter have frequently been criticized because their accuracy is gradually impaired through a loss of elasticity. Von Recklinghausen recommends controlling the instrument from time to time by comparing it with a mercury or water manometer. The instrument is supplied with a conveniently arranged cuff, 13 cm. wide, covered on the outside with canvas. The cuff is distended not by means of a rubber bulb, but by means of an air-pump fixed with the foot and worked by hand. To preserve sufficient excursions of the indicator with the oscillating pressure measurement the pump is not connected directly with the cuff and the manometer, but a capillary metallic tube is interpolated so that the pump chamber does not diminish the pressure oscillation. The tonometer is graduated in centimeters of water, instead of millimeters of mercury. Von Recklinghausen considers that this conforms better to the gram centimeter system recently introduced in physics, and he finds a practical value in this sort of graduation, because the specific gravity of water varies so little from that of blood, so that a simple addition or subtraction corresponding to different levels is sufficient for a rapid calculation of the pressure at any point of the vascular system. The low pressure values in the veins and capillaries are naturally more easily measured by water than by mercury pressure. To calculate the pressure found in accordance with the height of the heart, von Recklinghausen considers that the latter corresponds to a sagittal axis of the thorax drawn through the lower end of the sternum. When measuring in the sitting posture, the middle of the cuff upon the arm corresponds approximately with the height of the heart, which obviates the necessity for hydrostatic calculation. The disadvantage of this instrument is, however, that the figures differ from the usual values expressed in millimeters of mercury, and the mercury manometer will probably remain the instrument of choice for blood-pressure work. For the sake of comparison with the mercury manometer, it would be desirable to add to the instrument a scale graduated in millimeters of mercury. This instrument can be utilized just as any other manometer for the palpatory measurement of the blood-pressure. (See p. 117.) For

[1] See Martin, Münch. med. Woch., 1903, No. 24, p. 1021.

this, von Recklinghausen especially recommends the so-called oscillatory measurement, making use of the size of the oscillations which the manometer exhibits under the influence of the pulse. The minimum pressure is estimated in this way, according to von Recklinghausen, and corresponds to the lowest pressure upon the cuff, which makes the indicator show the greatest excursions. If the pressure be increased, the point at which these maximum excursions begin is ordinarily sharply marked;

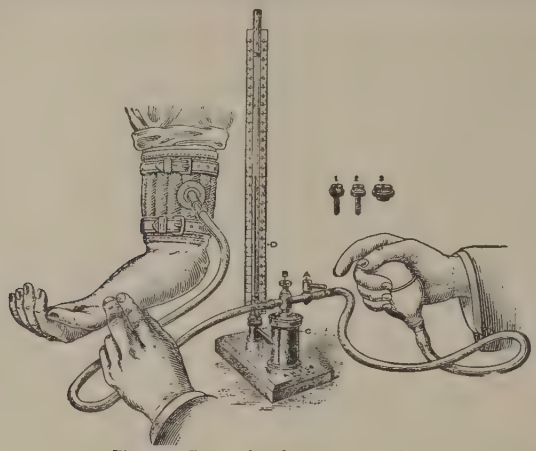


Fig. 97.—Stanton's sphygmomanometer.

sometimes, however, the oscillations increase indistinctly, even sufficiently to extend over 10 to 15 cm. of water. The maximum pressure is also estimated by these oscillations, and corresponds to the point at which the large oscillations produced by increasing pressure become suddenly smaller again. This boundary point, however, is less distinctly marked, and, therefore, von Recklinghausen recommends for estimating the maximum pressure this method, and in conjunction with it the old palpatory method (estimation of the cuff pressure at which the radial pulse disappears). His apparatus is also supplied with a device (tonograph), by means of which the oscillatory measurement can be represented graphically. There is also furnished a peculiar ring-shaped rubber pelotte, closed in the middle with a glass plate for vision. By means of this contrivance von Recklinghausen estimates the pressure at which the veins collapse (*venous pressure*), or at which the skin becomes pale from compression of the capillaries (*capillary pressure*).

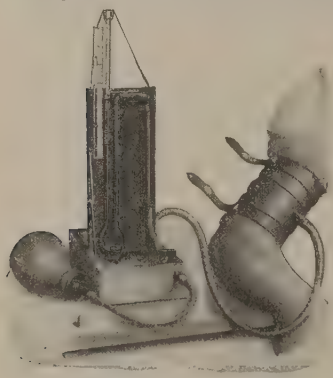


Fig. 98.—Janeway's sphygmomanometer.

Stanton's Sphygmomanometer.—Stanton's[1] instrument is shown in Fig. 97. The manometer consists of a metal cistern (*C*) connected with a glass upright tube and scale (*D*), which can be unscrewed for carrying. The armlet is a hollow rubber bag, 4 in. (10 cm.) wide and 16 in. (41 cm.) long, closed at both ends, and attached to an outer cuff of thick canvas, reinforced by tin strips. A wider cuff, 6 in. (15 cm.), is supplied if desired. A single rubber bulb is used for inflation. At *A* is a stop-cock, and at *B* a screw valve for the gradual lowering of pressure. It is a portable, convenient, and durable clinical instrument.

Janeway's Sphygmomanometer (Fig. 98).—Its special feature is the portable U-tube manometer attached to a case, into which it folds for carrying. The armlet

[1] W. B. Stanton, Univ. of Penna. Med. Bull., 1903, vol. xv, p. 466.

is a hollow rubber bag, 12 x 18 cm., loosely covered and attached to an outer leather cuff, 15 x 33 cm., which fastens by two straps with friction buckles. For inflation a Politzer bag with valve is used. *E* is a stop-cock provided with a needle valve, by which the pressure can be reduced gradually. It is a portable, convenient clinical instrument.

Repairs to the last named are frequently necessary, and the original cost of both these instruments is greater than desirable for an instrument so generally employed. Any one can construct a perfectly satisfactory apparatus for office and ward work at a cost of less than five dollars by purchasing a good cuff,[1] bulb, rubber tubing, glass T-tube, and U-tube manometer. The latter can be fastened to an upright board with a scale marked upon it, and nailed to another horizontal board.

Erlanger's sphygmomanometer[2] is, undoubtedly, the most accurate and valuable instrument yet constructed. It gives readings both of systolic (maximum) and diastolic (minimum) pressure, and therefore makes possible the calculation of exact mean arterial pressure. Fig. 99 shows the apparatus in perspective. The cuff is 12 cm. wide.

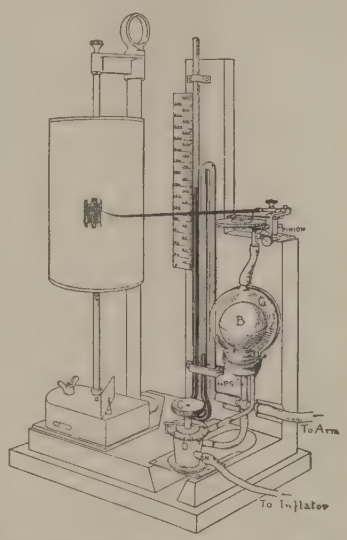


Fig. 99.—Erlanger's sphygmomanometer.

Besides the manometer, compressing armlet, and inflator it contains a somewhat elaborate reading mechanism and kymographiondrum. This mechanism consists of the tambour, the interior of which is connected with the air-chamber inside the glass bulb *G*. This air-chamber has no other openings while the record is being made, but automatically connects with the outer air through the tube *E* and the stop-cock *C* when rapid changes in pressure are made, which might damage the tambour. The pulse-waves are transmitted through the tube to "*P S*" and cause variations in volume of the rubber bulb *B*. These pulsations of *B* are, of course, reproduced by the air within *G*, and thus carried to the tambour, which inscribes them on the smoked cylinder. The purpose of the rubber bulb *B* is to shield the tambour from too sudden and great variations of pressure. The stop-cock is an important mechanism, but cannot be described intelligently without mechanical drawings. It is easily understood from the instrument itself. Unfortunately, this apparatus is too bulky to be carried far, and is more complicated than desirable for strictly clinical work. For purposes of physiologic experiment on human beings, and whenever very accurate readings of both pressures are desired, it should be the choice.—Ed.]

The Diagnostic Signification of the Measurement of the Systolic Arterial Blood-pressure

The introduction of these methods of estimating arterial (maximum) blood-pressure into clinical work gave promise of much assistance in functional diagnoses directly applicable to treatment. There arose, in particular, a tendency to settle the very important functional diagnosis of the existence of stasis by means of the height of the arterial (maximum) pressure, and to regard the existence of a high pressure as proof of a good circulation, an efficient heart action, and a contraindication to digitalis, and that of a low blood-pressure, on the contrary, to the use of the drug. This conception was, however, soon proved to be erroneous, and the author was the first to disentangle these complex relations by creating the idea of "*high-pressure stasis.*" He showed at the Congress for Internal Medicine (Berlin, 1901)

[1] [Galante Fils, rue de l'Ecole de Médecine, Paris, make the most convenient and durable cuff which I have used.—Ed.]

[2] Erlanger, J., Amer. Jour. Physiol., 1904, vol. x, Proceed. of Amer. Physiol. Soc., p. 14.

that the presence of a high arterial blood-pressure does not exclude the coexistence of stasis (inefficient heart action, retarded circulation, abnormal distribution of the circulating blood); and that a large group of cases with stasis, on the contrary, do exhibit a high maximum pressure: (1) for the most part, cases in which a primary increase of resistance in the vessels causes the stasis, *e. g.*, in arteriosclerosis and chronic nephritis; and (2) other cases in which the dyspnea caused by the stasis leads to the stimulation of the vasomotor center and therefore secondarily causes a high blood-pressure. This, the author's "high-pressure stasis," in which a diminished heart efficiency exists in the presence of high arterial pressure, is an apparent paradox, but it may be thus explained: with the increased vascular resistance even very small systoles suffice to maintain the high blood-pressure, and if the systoles be small, the high pressure is perfectly consistent with insufficient heart power, because the heart work of a systole is measured by multiplying the volume of blood expelled by the resistance to be overcome. This reasoning indicates that a high blood-pressure is not always a contraindication to the use of digitalis which increases the heart power and improves the systole. Besides practical experience with such cases of "high-pressure stasis" proves that digitalis lowers rather than raises their blood-pressure. Neither is a low blood-pressure always a sign of a poor circulation. Fever, where the circulation is probably accelerated, is an instance in point; because very likely an increased and exceptionally good circulation may accompany even a low blood-pressure provided that relaxation of the vessels diminishes the resistance. In fever, *e. g.*, in pneumonia, a low pressure in itself is by no means an indication for the use of digitalis, although one may employ it as a prophylactic measure.

The determination of blood-pressure is, therefore, evidently not so valuable in functional diagnosis of the circulation as was originally expected. Nevertheless, its measurement does possess some diagnostic significance, as, for example, the frequent occurrence of high pressure in chronic nephritis and of low blood-pressure in fever. In febrile conditions the height of the blood-pressure has a certain prognostic significance, in that the exient of the lowering corresponds in some measure to the severity of the constitutional disturbance. This is especially the case in pulmonary tuberculosis, where the toxemia often shows itself in a lowering of the blood-pressure to 80–100 mm. before causing fever. This can be easily explained by the fact that the febrile manifestation is often retarded on account of the small amount of combustible material furnished by a reduced diet. (See p. 71.)

The "absolute sphygmogram" (see the following section), and in particular the comparative determination of maximum and minimum pressures, furnish somewhat more valuable information, but by no means as valuable as the beginner would have believed.

THE ABSOLUTE SPHYGMOGRAM

The Significance of the Simultaneous Determination of the Systolic (Maximum) and the Diastolic (Minimum) Arterial Blood-pressure; the So-called "Pulse-pressure" (Height of the Absolute Sphygmogram) and the Blood-pressure Quotient

We have already pointed out in the section on Sphygmography the imperfections of this method. The data derived from the form of the curve are by no means satisfactorily definite. The significance at first attributed to the secondary elevations (Landois, Marey, and others) has been disproved by the later investigations of v. Frey and Krehl. (See p. 133 et seq.) Even the general form of the sphygmogram cannot be easily interpreted since (1) the form of the summit of the curve is influenced greatly by reflected, partially retreating waves, and (2) the height of curve depends on many adventitious factors (mode of application of the sphygmograph, tension of its spring, flexibility of the arterial wall, width of the artery, frequency of the pulse, etc.). Consequently the height of the sphygmogram not being a reliable criterion, the method furnishes but little useful information in regard to the size of the pulse or of the pulsatory changes in arterial pressure that are, of course, points of greatest clinical interest; nor does it afford any means of determining the manner of the rises or drops of such pressure. It throws therefore but little light upon the question of the celerity or tardiness of the pulse. For instance, it is frequently difficult to demonstrate the pulsus celer from the sphygmogram of a patient in whom its presence is absolutely proved by palpation, the capillary pulse, and the tone of the arteries.

This leads to attempts to obtain the excursions of the pulse by the direct measurement of the maximum and the minimum pressures. For a criticism of the experiments

made with this purpose by Potain.[1] Hensen,[2] and von Recklinghausen,[3] see the author's article on the absolute sphygmogram.[4] In the latter the author reported a new method of obtaining the minimum pressure, which he afterward found had been previously described by Janeway,[5] and which was later, independently of Janeway's communication, worked out by Masing,[6] Strassburger,[7] and himself.[8] The fact that four writers should independently have fallen upon the same method ought to speak well for the correctness of its principle. This method consists in measuring both the maximum and minimum pressures by means of the ordinary sphygmomanometer. The maximum pressure corresponds to that which obliterates the arterial pulse, the minimum pressure to that under which the pulse first begins to decrease in size. All four authors mentioned used Riva-Rocci's instrument, and all but Strassburger, who employed palpation, determined the moment when the size of the pulse began to decrease, by making sphygmograms from the radial artery. For a proof of the assumption that the minimum pressure corresponds in time to the moment when the pulse becomes smaller, see the author's article mentioned above. Evidently the instant the pulse becomes smaller, the compression of the bag must begin to block the transmission of the pulse-wave from the brachial to the periphery; and this hindrance must act not only in a beginning compression of the artery, naturally corresponding in time to the moment when the arterial pressure is lowest, *i. e.*, the valley of the wave; but as soon as the pulsation increases the pressure, the hindrance (compression) is again overcome. When the compression is still further increased, the pulse-wave will completely disappear at the periphery, and at this moment the maximum or systolic pressure can be read upon the manometer scale. (See p. 164, et seq.) The author in the above-mentioned article has also supported the assumption that this is the actual maximum pressure.

One difficulty met with in this procedure is that, when the cuff of the Riva-Rocci apparatus is inflated, the resulting venous congestion elevates the spring of the Jaquet's sphygmograph. This raises the tracing needle and so shortens the ordinates of the curve. Moreover, the spring being lifted somewhat does not truly appreciate the pulse-wave. Hence with increasing pressure in the cuff the venous pressure gradually diminishes the height of the wave. It is difficult to distinguish such a lowering of the curve, due to a secondary effect of the apparatus, from that caused by the initial compression of the artery.

This difficulty may be corrected, at least in part, by applying the sphygmograph as tightly as possible in the beginning, since then the swelling of the extremities caused by the venous congestion will not materially increase the pressure against the frame and so raise the spring. To prevent the artery from being compressed by this congestion the author fastens a "cross bow" to the sphygmograph frame to which the straps are applied, and this device (already described upon p. 125) allows the artery to lie in a sort of hollow trough and prevents any pressure despite the fact that the wristlet is buckled on very tightly. The cross bow is so arranged that it can be applied or taken off at will. A satisfactory substitute for this cross bow can be improvised by slipping under each arm of the frame at the upper extremity of the wristlet a rounded piece of cork. Elevation of the curve dependent upon inflation of the cuff can be much reduced by thus tightly buckling the cuff, or even wholly prevented if we inflate the cuff more rapidly than the arm can swell. The direct pressure of the radial artery's venæ comites upon the spring inevitably produces some little rise in the curve in most instances. If slight, however, this is of no disadvantage, because, in spite of it, the reduction of the height of the pulse-wave, by increasing the pressure in the cuff, is easily recognizable (Fig. 100, at the mark 100.) To decide whether this reduction depends entirely on the raising of the curve, a curve may be traced without pressure in the cuff, the position of the recording needle being gradually raised by the screw. This will show what influence the raising of the curve in and of itself has on the height of the single pulse-wave. Ordinarily, no effect is visible so long as this rise is not too great. Moreover, before each increase of pressure in the cuff the clockwork of the sphygmograph may be stopped and the needle returned to its original position, so that each separate section of the curve

[1] Le pression arterielle de l'homme, Paris, Masson, 1902.
[2] Arch. f. klin. Med., 1900, vol. lxvii.
[3] Arch. f. exp. Path. u. Pharm., 1901, vol. xlvi.
[4] Arch. f. klin. Med., 1904.
[5] University Bulletin of the Medical Sciences, 1901, vol. i, No. 3.
[6] Deut. Arch. f. klin. Med., vol. lxxiv.
[7] Zeit. f. klin. Med., vol. liv
[8] Deut. Arch. f. klin. Med., vol. lxxi, 1904.

corresponding to a single pressure will be written at the same height as every other section. After a certain amount of practice this technic can be performed by the examiner alone, although assistance simplifies the task. The pressure is increased 10 mm. at a time, and each increase indicated on the sphygmogram. These marks may be very conveniently registered by the pneumatic registering apparatus of the simplified Jaquet instrument (p. 128) or by Mackenzie's polygraph (p. 129). After the minimum pressure has been determined by noticing the place at which the height of the sphygmogram is suddenly decreased, the pressure should be increased until the curve becomes a straight line, thus indicating the maximum pressure.[1]

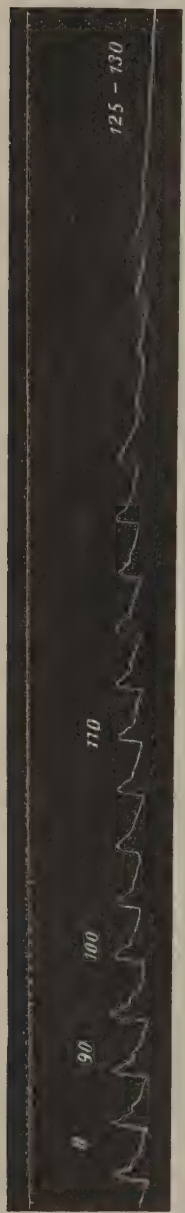


Fig. 100.—Determination of the maximum and the minimum pressure.

In regard to the criticisms of this method, based upon Fellner's and Rüdinger's experiments on animals, see p. 167.

The method recommended by Janeway, Masing, and the author for estimating minimum pressure has been recently modified by K. Schliak (Zeitschrift für physikalische und diätetische Therapie, 1908, 1909, vol. xii). Instead of showing through the diminution of the sphygmogram the diminution of the pulse at the moment when the minimum pressure begins to compress the artery by means of the cuff, this investigator measures the excursions of the writing needle of the sphygmograph directly upon a millimeter scale. He employs the Jaquet sphygmograph, and has printed upon the end of the paper strips, vertical to their length, a millimeter scale, which he protects from being smoked by covering with a piece of paper. These strips can be obtained from C. G. Naumann, Seeburgerstrasse 57, Leipsic. After the application of the Riva-Rocci apparatus Schliak uses the sphygmograph in the ordinary way until the needle reaches the unsmoked part of the paper. He then stops the instrument and reads off the minimum pressure at the moment when, with increasing pressure of the cuff, the writing needle begins to make smaller excursions upon the scale. The maximum pressure can be read off in the same way at the moment when the writing needle makes no more excursions upon the scale. He claims that the instrument has this advantage over the graphic method recommended by Janeway, Masing, and the author, that the measurement can be repeatedly controlled without difficulty. On the other hand, the procedure loses its objective documentary character.

In this way we obtain the maximum and the minimum pressure of a sphygmogram in absolute values, and if we employ a sphygmograph with a time-making apparatus like Jaquet's, we can also correlate the individual components of the curve, and from all these data construct what the author calls an "absolute sphygmogram." This he understands to mean an artificial sphygmogram, which is so accurately proportioned that at every point the ordinates correspond to the pressure. In its simplest form the secondary elevations are disregarded, and the skeleton of the wave depicted, showing the shape of the main summit and the steepness of the ascending and descending limbs, *i. e.*, the position in relations of time of the main summit to the valley ("reduced absolute sphygmogram").

[1] If the pelotte manometer be used for determining the maximum pressure, the minimum pressure may be determined, at least approximately, by obtaining the pressure by palpation the moment when the pulse-wave becomes smaller (Strassburger's method).

Fig. 101 shows the method of constructing an absolute sphygmogram upon ordinary millimeter paper. A single wave is measured along a horizontal base line, *aeb*, each centimeter of the paper corresponding to the ⅛ second of a Jaquet sphygmograph. If, for example, each pulse-wave correspond to ⅛ of a second (4 cm.) (8 of the squares), *a* to *b* are marked off. From each of these points is erected a vertical *ac*, *bd*, the length in millimeters of which corresponds to the minimum pressure, *e. g.*, 100 mm. Hg. The point *e* is determined from a sphygmogram of the pulse traced at high speed by measuring the distance from the foot to the summit along the horizontal. From *e* is erected another vertical *ef*, whose length corresponds to the maximum pressure. Then, by connecting *c* and *d* with *f*, the absolute sphygmogram in its simplest form is completed. From Fig. 101, *e. g.*, we see at a glance that the wave began with a pressure of 100 mm. and fell to the minimum again in about 0.68 second. The difference in height between *c* and *f* (*ef–ac*) is called by the author the *height of the absolute sphygmogram* (pulse-pressure, see p. 178).

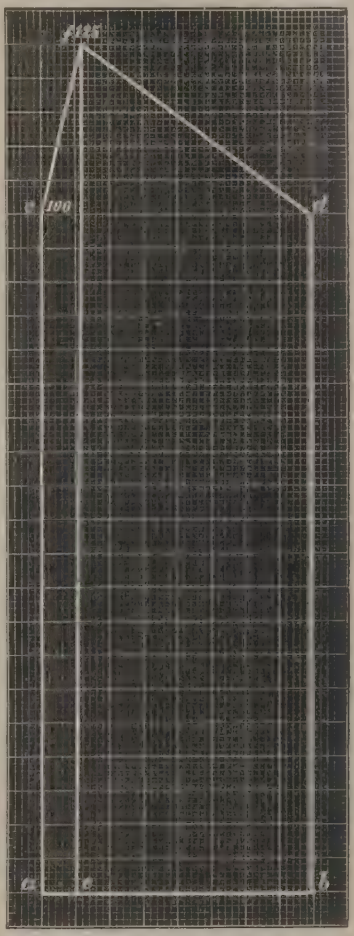


Fig. 101.—A reduced absolute sphygmogram in its simplest form.

This simplified absolute sphygmogram can easily be made more elaborate by representing in similar fashion the secondary elevations and depressions of the pulse-curve. The time of each is obtained from the ordinary sphygmogram (made with rapidly moving paper), and the height computed by finding the ratio between the height of the particular elevation under consideration and the maximum height on the ordinary sphygmogram, and plotting it out on the millimeter paper. The points of the secondary apices and depressions can then be connected by a curve which should closely resemble that of the ordinary sphygmogram. There appears, however, to be no particular advantage in such an elaboration.

The absolute sphygmogram obviously gives a correct picture of the blood-pressure in the arterial system, drawn to an absolute scale. The pressure in the aorta probably differs very little from that in the radial artery, as there is so little friction to be overcome between the aorta and the wrist.[1] The rate of the pulse-wave also is practically the same, so that the absolute sphygmogram of the radial artery may without any great error be taken as that of the aorta. The practical clinical uses of the absolute sphygmogram are not, however, so extensive as might be at first supposed. It has been found impossible, for example, to draw from it conclusions concerning the strength of the cardiac activity or of the systoles (see the author's own discussion in his work already referred to). Strassburger's[2] criticisms, however, have not shaken the author's conviction of the correctness of his procedure. He admits that Fellner's[3] conjecture concerning the influence of the vis-

[1] Tigerstedt, Lehrbuch der Physiologie der Kreislaufes, Leipsic, Veit und Cie, 1893.

[2] Deut. Arch. f. klin. Med., vol. lxxxii and lxxxv.

[3] Arch. f. klin. Med., 1905, vol. lxxxiv.

cosity of the blood on the absolute sphygmogram may be correct. From the absolute sphygmogram conclusions may be drawn concerning the fluctuation of blood-pressure, the volume of blood expelled at each systole, and the condition of contraction of the arteries. The practical significance of the absolute sphygmogram lies in the possibility of a correct decision in regard to rapidity or slowness of the limbs of the pulse-wave (celerity, tardiness). In the absolute sphygmogram the difficulties arising from the unknown values of the ordinates of the curves (p. 141) are eliminated. As far as the form of a single wave is concerned, the absolute sphygmogram, instead of being simply a means of demonstration, becomes a valuable diagnostic help. It is the only means at hand to support the diagnosis of an aortic lesion by a certain demonstration of a pulsus celer or pulsus tardus. The celerity is measured by the angles which the ascending and descending limbs make with the horizontal.

It is possible that Mackenzie's differentiations of fevers into those with a more and those with a less favorable prognosis (the sthenic and the asthenic form, p. 148) based upon the more or less strongly pronounced diastolic sinking of the blood-pressure relative to the condition of dicrotism, may become of greater significance if the absolute sphygmogram be used. Strassburger considers that the greatest use of the absolute sphygmogram is to determine the *blood-pressure quotient*, which he defines as the quotient obtained by dividing the amount of pressure variation (the "pulse pressure") by the maximum pressure. The author's critical analysis of the absolute sphygmogram argues against the far-reaching inference which Strassburger[1] draws from the blood-pressure quotient and applies to the circulation.

THE MEASUREMENT OF THE VENOUS PRESSURE

In view of the fact that the measurement of the arterial blood-pressure alone affords by no means satisfactory conclusions regarding the condition of the circulation, it would obviously be of advantage to determine also the venous pressure. As a matter of fact, the venous pressure is quite as important a factor in circulatory conditions as is the arterial, because in accordance with hydraulic laws the rapidity of the blood-current depends upon the difference in pressure between the arteries and the veins.

Gärtner,[2] assuming that the veins act like manometer tubes opening into the right auricle, attempted to measure the venous pressure in the right auricle by having the patient raise his arm until a clearly visible vein, *i. e.*, one on the back of the hand, began to empty itself. The difference in height between the level of the spot observed and the right auricle gave the pressure at the auricle in centimeters of water, since this pressure is obviously what must be overcome to enable the vein to empty itself. In ordinary conditions the pressure is practically nil or even negative, so that the vein will empty itself when on a level with the auricle (at the fifth rib, in Gärtner's calculations); but in conditions of stasis the pressure is so much increased that the arm must be raised.

This method, though apparently very plausible, has certain flaws. In the first place, the pressure at the right auricle is a variable quantity, changing every moment with the phase of the heart's action, with the auricular contraction, and even with the ventricular activity. If the phenomenon in the vein be taken to mark the normal or minimum pressure at the auricle, it may be answered that the variations of the auricular pressure reach the small veins only very slowly and incompletely, otherwise we should normally always observe a venous pulse. It must, therefore, be assumed that the hydrostatic pressure in the vein works, not directly against the auricular pressure, but against a certain average pressure in those veins into which the small vein in question empties. In the second place, it is obvious that the emptying of the vein depends not merely on the pressure exerted against it, but also on the mass of blood flowing into it from the arteries. The vein is not, as Gärtner considers it, a mere manometer, because no such reflux exists in these tubes. It is obvious that in some cases, despite a low pressure at the auricle, the vein might not visibly collapse simply on account of the large amount of blood flowing into it. So that this method measures neither the pressure at the auricle nor the pressure of the vein into which the vein in question empties, especially as on account of the manifold anastomoses, it is impossible to tell what vein that would be. Although a critical analysis shows that the relations in Gärtner's method are too complicated to be employed as an accurate measure of venous pressure, yet the author does consider the phenomenon of some clinical value. If the veins of the

[1] Strassburger has more recently modified his views. Arch. f. klin. Med., vol. lxxxv.

[2] Münch. med. Woch., 1903, No. 47.

arm do not empty until the arm is markedly elevated, some venous stasis evidently exists, and vice versâ. The author considers, however, that the jugular veins are more trustworthy witnesses to speak for venous stasis, because when they collapse, we are certain that their blood empties into the innominate veins. Hence when the upper half of the body is raised and the jugular veins previously noted to be congested are seen to collapse, we are certain that the hydrostatic pressure in the innominate veins has been overcome. In this general sense, the collapse of the jugular veins may be utilized in the clinical diagnosis of stasis, but no exact measure can be expected for the reasons cited above, and principally because of the arterial blood-supply.

Oliver,[1] von Basch,[2] A. Frey,[3] and Sewall [4] have all attempted to measure the venous pressure directly, the principle of all their methods being essentially the same. Von Basch places a glass vessel open below over a superficial vein on the back of the hand and raises the pressure in the vessel until the vein collapses. The pressure exerted equals that in the vein at that moment.

Von Frey also uses a vein on the back of the hand, the arm being abducted and the hand held at the level of the right auricle, which he estimates as that of the third rib. He compresses the vein by means of a solid pelotte with a measured pressure, stroking it empty from the pelotte in a centripetal direction. In case the blood reflux is not prevented by a valve, one compresses the vein with the finger at some distance centrally from the pelotte. The vein then remains empty until the pressure in the pelotte is decreased to an amount which the blood coming from the periphery can just overcome. This pressure obviously equals the venous pressure at the point in question. Von Frey uses a metal pelotte and a kind of spring-balance arrangement which measures the pressure in grams (like Verdin's sphygmometer, p. 163). He finds the average venous pressure in health on the back of the hand to be 10–15 gm., in elderly people somewhat more, but he gives no figures in pathologic conditions. The same criticisms are to be made on the use of a spring pelotte here as in measuring the arterial pressure. (See p. 163.) The results cannot be correct, because the pressure as estimated is influenced by the caliber of the vein compressed. Sewall has improved the method somewhat by using a hollow elastic air-cushion.

The author has modified the method by using an air pelotte and a manometer. Owing to the small amounts of pressure to be measured he substitutes a manometer filled with colored water instead of mercury, the bore of which should be large enough to prevent any error from capillary action (3–4 mm.). It is difficult to observe the vein and the manometer simultaneously. A good plan is to have them both in the same line with the eye, and glance at the vein every time the water in the manometer falls a centimeter.

Von Recklinghausen [5] has recently invented a similar method, but one which involves more complicated apparatus. He found that the pressure in a vein of the hand is practically equal to that of a blood-column the height of which equals the vertical distance between the position of the hand and the sternoclavicular joint.[6] So that if one subtract the pressure due to the weight of this column, the pressure in the veins of the hand is practically nil. Naturally, in judging the condition of the circulation only the pressure in the veins where they enter the thorax need be considered, and this also is practically nil. The author's results do not verify these conclusions. He found the pressure often several centimeters of water above or below the value thus reckoned. He also believes that the variations in the venous pressure during the few minutes of observation depend not so much on the variations of arterial pressure as on the changes in the caliber of the smallest vessels and the veins themselves.

In stasis the venous pressure in the hand may be considerably raised, but not necessarily so, owing to the great power of dilatation and accommodation on the part of the venous walls. The author has repeatedly seen cases of high-grade cardiac stasis where the venous pressure was normal. The visible dilatation of the veins is a surer sign of stasis, but even this may be due to an increase in intrathoracic pressure (emphysema, pleurisy, pneumothorax).

[1] Blood and Blood-pressure, London, 1901.

[2] Von Basch, Wien. med. Presse, 1904, p. 911, and Arch. des Sciences Biologiques, St. Petersburg, vol. xi, Supplement, 1904, p. 117.

[3] Encyklop. Jahrb. der ges. Heilkunde, new series, vol. iii.

[4] Jour. Amer. Med. Assoc., October 20, 1906.

[5] Arch. f. exp. Path. u. Pharm., 1906, vol. lv, p. 468.

[6] This is the location of the highest point of the course of the veins leading from the hand to the heart.

MEASUREMENT OF THE CAPILLARY PRESSURE

Von Kries[1] was the first to measure the capillary pressure in man. He placed a weight on a glass plate laid on the skin, and estimated the pressure necessary to produce pallor. R. Roy and J. Graham Brown have made similar experiments on the frog's web. Von Basch[2] endeavored to make the measurement of the capillary pressure clinically useful. He applied an air-tight glass bell to the skin, and increased the pressure in it until pallor was produced. Von Recklinghausen[3] employed the same method as in his measurements of the venous pressure, using a transparent pneumatic pelotte, and employing the blanching of the skin as an end-reaction. None of the methods produce practical results to be depended upon. The blanching of the skin appears gradually, showing that the pressure in some of the capillaries in the region under observation is greater than that in others. The pressures are so slight that the different individual resistances of the tissues play too important a part, more so even than in the measurement of the arterial pressure by Gärtner's manometric method (p. 170). The capillary pressure is also apparently much higher in some places than in others, which very materially detracts from the clinical value of such measurements.

SPHYGMOBOLOMETRY[4]

The attempt to estimate the condition of the circulation from sphygmomanometric measurements is as futile as it would be to try to calculate the horse-power of a locomotive, and even the speed of the train, from the measurement of the steam pressure in the boiler. Even the consideration of arterial pressure variations ("pulse pressure," height of the absolute sphygmograph) is of no help. A knowledge of the difference in pressure between the steam entering and the steam leaving the cylinders of an engine still leaves one in complete ignorance concerning the work of which the engine is capable.

The author, therefore, believes it would be of great service to endeavor to measure *not the blood-pressures, but the energy of the pulse-wave, and so, indirectly, the strength of the systole.* For this purpose he has constructed an instrument, the sphygmobolometer, about to be described.[5] As in the measurement of the blood-pressure, the Riva-Rocci cuff with the author's quicksilver manometer is employed. It is necessary that as much as possible of the energy of the pulse-wave shall be transformed into measurable pulsatory movements of the mercury in the manometer. To lessen the friction, a larger tube (5 mm. bore) is used than in the measurement of the blood-pressure. This also enables a float to be placed in the longer limb of the manometer. In order to get a vigorous movement of the mercury a somewhat larger cuff should be used (8 cm. broad). The objection to the very broad ones used by von Recklinghausen in pressure measurements (13 cm.) is that they have to be applied to the arm spirally, so that the amount of surface actually in contact with the arm differs with the caliber of the arm, making it impossible to compare the results of experiments on different individuals. Only a cuff circularly applied gives a constant area of contact

[1] Verhandlungen der sächsischen Gesellschaft d. Wissenschaften math.-phys. Classe, 1875, vol. xxvii, p. 149.

[2] Wien. klin. Rundschau, 1900, No. 28 and 29.

[3] Arch. f. exp. Path., 1906, vol. lv.

[4] See Sahli, Deut. med. Woch., April 18, 1907, No. 16 and 17. The sphygmobolometer is still in process of manufacture, so that it cannot be given to the public until later.

[5] The name is derived from βόλος, "a throw." The author considered the names cardiodynamometer or sphygmodynamometer, but discarded them because they might easily lead to misconceptions of the essential nature of the new method.

between the skin and the cuff, and for this method of application the cuff must not be too wide, on account of the variations in the curvature of the arm. It is convenient to have the cuff connected with a small escape-tube fitted with a stop-cock, so that the pressure in the cuff may be diminished at will, and also to have a stop-cock interposed between the manometer and the bulb. The author employs a four-armed glass tube arranged as in the following diagram (Fig. 102.)

The cuff is applied to the patient's arm in the usual way, and the pressure gradually increased; at each increase of pressure communication between the bulb and the cuff is temporarily shut off, either by using a stop-cock, as above, or by pinching the tube. When a certain pressure is obtained, the mercury in the manometer will be seen to oscillate up and down. Sometimes these oscillations are visible when communication with the bulb is open, but generally they are plainer when the bulb is shut off. Some investigators have employed these oscillations to determine the pressure, *e. g.*, von Recklinghausen, in his "Treppencurven," and Mosso (see the third edition of his text-book, 1902, p. 128). They obviously arise from the energy of the pulse-wave, which, at a certain medium point of compression of the brachial artery, is carried through the cuff to the manometer in sufficient strength to set the quick-

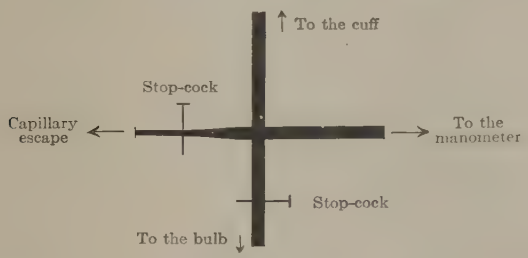


Fig. 102.

silver in vibration. If the bulb be connected, the amount of air it contains, of course, materially reduces or even hides the periodic increase of pressure in the air between the pulse and the manometer. The smaller the caliber of the connecting tube and the more rigid its walls, the stronger, of course, are the pulsations. The point of pressure at which the maximum vibrations are set up in the manometer is found not to correspond to that of the maximum nor to that of the minimum arterial blood-pressure, but to lie somewhere between these, not, however, at their exact mean. This is contrary to the principle involved in Mosso's and other instruments, according to which the point at which the mercury vibrations are greatest is taken to be that of the minimum arterial pressure. As a matter of fact, experiments show that it lies between the maximum and minimum, varying with the form of the pulse-wave. In many cases it falls at no one fixed point, the mercury vibrations remaining at a maximum through a considerable range of pressure. In such cases von Recklinghausen assumes that the lowest pressure at which the maximum vibrations occur corresponds to the minimum pressure in the artery.

The author's proposed use of mercury vibrations has nothing in common with conclusions as to the state of the blood-pressure; nor is

it related to the attempts of Riva-Rocci and others to employ these vibrations in the determination of the lateral arterial pressure, a concept by no means clear to the author.

Sphygmobolometry is entirely different; it aims to determine, not the pressure, but the work performed by the pulse. The vital energy of the pulse-wave, which is transferred to the cuff, is what sets the column of mercury in vibration. If that point of compression be selected where these vibrations are at a maximum, *i. e.*, where the transformation of energy is most nearly complete, the work done by the pulse-wave can be calculated after reading off the maximum height of the mercury column. Obviously, however, such conclusions hold good only for one type of apparatus, the results being influenced by the breadth of the cuff, the volume of air-space inclosed, the quality of the rubber, etc. In his original communication[1] the author attempted to announce absolute results concerning the work done by the pulse-wave, but it must be understood that the values thus obtained were always to be multiplied by the constant of the particular instrument. If, however, instruments of the same construction are always employed, as is desirable for clinical work, this constant may be ignored, and at least relatively correct and comparable results be obtained.

One other important point must be noted. Since the maximum excursions of the mercury do not occur at the moment when the manometer shows the maximum pressure, it is obvious that a part of the pulse-wave escapes under the cuff. The author has shown that this fraction is variable, depending upon the shape of the pulse-wave.[2] In order, then, to secure constant conditions the wave must be prevented from escaping in part under the cuff, and as far as possible be forced to exert its energy entirely in the direction of the manometer. This is accomplished by first winding an Esmarch bandage around the arm, either at the elbow or between it and the cuff, tightly enough to obliterate the radial pulse. This device to a certain extent converts that portion of the brachial artery which extends to the lower edge of the cuff into a culdesac from the aorta (a sort of sphygmoscope).[3]

If, now, the energy of the pulsation be noted at this arterial stump and be measured by the excursions of the mercury, we approximately estimate the energy of the aortic pulse. The instantaneous compression of the venous trunks, caused by the pressure of the cuff, subjects not only the small veins and the arteries, but also the capillaries, to the arterial pressure, and they all pulsate with it. This naturally facilitates the completeness of the transference of energy to the mercury, since not only the small volume of the arteries, but the whole arm stump, takes part in the variations of volume. The mechanical conditions of the test are the same in every case; hence it seems proper to assume that practically constant and comparable estimates are obtained, provided, of course, that the pressure of the cuff be adjusted to secure maximum excursions. In making use of this test clinically we must evidently avoid any factor which could artificially alter the energy of the pulse-wave, *e. g.*, pain from an overtight Esmarch bandage, such as to affect the heart action. Caution, experience, and quickness in performing the experiment will, however, usually eliminate this particular factor.

[1] Deut. med. Woch., 1907, No. 16, et seq.
[2] Deut. Arch. f. klin. Med., 1904, vol. lxxxi.
[3] See Marey, La circulation du sang, 1881.

It remains, therefore, merely to measure the extent of the excursions of the mercury, and to make the calculations from the data obtained. For the measurement of the excursions of the mercury, it is sufficient for purely practical clinical or demonstration purposes merely to note with the eye the highest point on the manometric scale reached by the mercury. The distance must, however, be read to fractions of a millimeter. For this purpose a scale giving fifths of a millimeter may be fastened alongside the mercury tube, and by means of a suitable telescope, the extent of the excursions be read off from a distance. For more exact purposes a graphic method of recording the results is preferable. This might be done by connecting the air-space above the mercury with a Marey tambour, and recording the excursions pneumatically on the kymographion. In this method, however, the increase due to the lever action must be calculated each time and taken into account. The author, therefore, uses a float riding directly on the mercury and carrying a writing point, which records the excursions vertically, and without magnification. At first this float had an ordinary horizontal writing arm, which, by a small hanging weight, was held pressed gently against the writing surface. The latter consisted of any kymographion preferred, or the arrangement described on p. 126 (Fig. 49). In order to make the apparatus simpler for the practitioner, however, the author has contrived a writing surface which shall

Fig. 103.—The author's sphygmobolometer.

be a permanent part of the instrument, and render it independent of any kymographion.

This consists of a piece of smoked paper, 12 cm. high, fixed in a vertical frame attached to the stand of the manometer near its base. By turning a crank the paper and its frame can be moved horizontally about 6 cm. The manometer stand is so heavy at the base that this can be done without shaking the instrument. Since we are not concerned with the time relations of the pulse, but merely with the calculation

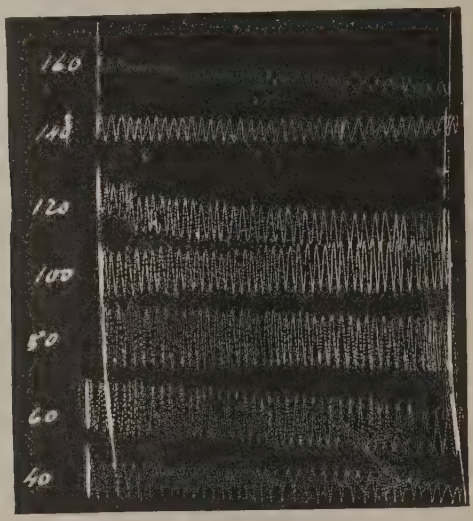


Fig. 104.—Sphygmobologram.

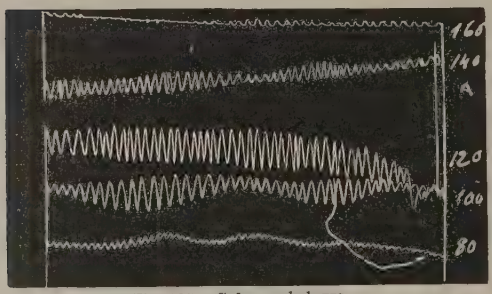


Fig. 105.—Sphygmobologram.

of its energy, it is not necessary to have any clockwork for moving the paper. Figs. 104 and 105 show what neat and regular curves may be obtained by moving the recording surface by hand. To facilitate the insertion of the paper, a joint in the base of the instrument permits it to be placed in an almost horizontal position.

As the writing apparatus, for the sake of stability, must be placed as near the base of the instrument as possible, it becomes necessary to devise some means for transferring the movements of the float from

the top of the manometer tube to the bottom. For this purpose several contrivances were tested, the best proving to be the one represented in Fig. 103. A thread *ab* is attached to the arm of the float. From it hangs a thin metal wire, *bc*, bent at its end into a horizontal writing point, *cd*. This wire is guided by being passed through the glass tube, *fe*, which is fastened to the instrument. The proper amount of friction can be attained by adjusting this glass tube and a greater or less torsion of the thread.

The technic of the procedure is as follows: the cuff is attached to the upper arm and connected with the apparatus by the 4-armed glass tube. (See Fig. 102.) The brachial artery distal to the cuff is compressed by an Esmarch bandage until the radial pulse disappears. By compression of the bulb the column of mercury with its float is made to assume different heights. After the proper adjustment of the needle to the smoked paper has been made, bolometric curves are taken for the different pressures, the connection with the bulb being each time cut off. A slow movement of the paper is sufficient, because the method is concerned with the height, and not the form, of the curve. Hence a large series of pulse-waves can be recorded on one line of a paper 6 cm. wide, and by moving the smoked paper back and forth curves for the different pressure heights may be traced one below the other. (See Figs. 104 and 105.)

With such long tracings we can often note distinct Traube's waves corresponding to a periodic increase and decrease in the mercury excursions. (See Fig. 105.) Fig. 104 does not show these waves. In such instances the cardiac work, and not alone the blood-pressure, is evidently increased and decreased.

The zero pressure line is given the position of the writing point when the manometer is at rest; the height of pressure corresponding to each curve can then be easily determined by measuring in millimeters the distance from the zero line to a horizontal drawn later to intersect the points half-way between the tip and foot of the waves. Since the manometer is constructed with two limbs, this distance must be doubled. It is self-evident that this doubling only applies to measuring the mean position of the mercury, not the height of an individual wave.

For reckoning the work done by the pulse under observation we select that curve which shows the greatest excursions,[1] since at that moment the transmission of energy was most nearly complete.

In the author's first article on sphygmobolometry he deduced the following formula for the *relative* work done by the single pulse-beat:

$$(1)\ W = h\,(h + H)$$

W = work done; h = amplitude (in millimeters of mercury) of the maximum sphygmobolometric excursion; H = height (in millimeters of mercury) of the corresponding manometric pressure. In exceptional cases other values are assigned to $h + H$. (See p. 186.)

The formula gives only a *relative* estimate of the work done, in the sense that the right-hand side of the equation holds good only for the comparison of value obtained by one and the same instrument in examining different cases. To determine an absolute value, the right-

[1] If Traube's waves be present, an average excursion must be selected.

hand side of the equation must be multiplied by a constant, in the calculation of which the specific gravity of the mercury, the diameter of the manometer tube, and various other factors in the construction of the instrument are concerned. For practical clinical use the relative value is all that is required. The author has shown in his original article that the oscillations due to inertia of the mercury do not affect the correctness of the formula. The entire work performed by the pulse in one minute is obtained by multiplying the work done by a single beat by the pulse-rate.

The measurement of the pulse amplitude (height of the absolute sphygmogram, pulse pressure) differs fundamentally in principle from the measurement of the pulse energy (value of work determined sphygmobolometrically and expressed in the equation cited above). It does not depend at all upon the pulse amplitude or minimum pressure, but corresponds to the work done at the artery and expressed by the formula $W = \frac{M \times v^2}{2}$ where M = the mass of the pulse-wave which impinges upon the cuff (dependent on its form, height, and duration, as well as on the caliber of the artery), and v = the velocity of the lifting components of the wave motion —quantities which do not enter at all into the static computation of the pressure relations.

To calculate the value of W in formula (1) we select for h and H those values which correspond to the sphygmobolometric curve having the greatest amplitude of the series, because the maximum excursion of the curve naturally suggests the most perfect transmission of the pulse. At any rate, it is certain that those curves which are obtained under a *lower* manometric pressure than the curve of the maximum mercury excursion represent a lower value of work done, thus indicating an incomplete transmission of energy, and are useless for this purpose. But the maximum work, it must be noted, is under some circumstances found by selecting, not the curve with the maximum amplitude (height of excursion, h), but rather one of those immediately above it, where the decrease in h (height of excursion, amplitude) is more than compensated for by the increase in H (pressure), *e. g.:*

h	H	W
6 mm	100 mm.	$6 \times 106 = 636$
5 mm.	125 mm.	$5 \times 130 = 650$

In general, however, it will be found that the value of h falls off so quickly that the increase in H is overbalanced, so that the maximum value of W usually corresponds to the maximum value of h.

It remains to consider the clinical value of the results obtained by sphygmobolometry. It is obvious that we are computing not the entire energy of the heart, but only that fraction which acts upon the portion of the arm stump obstructed by the Esmarch bandage and corresponding to the surface of the cuff. The muscular development of the arm would naturally affect this fraction to some extent. But in healthy individuals the differences between the results are found to be so small, and in pathologic conditions of the heart so great, that the author believes it possible to consider the result found as an approximately constant fraction of the total work done by the heart in each case. Conclusions may, therefore, be drawn concerning the entire amount of cardiac work—a result impossible by any previous method.

The objection may be made that we are measuring simply the *wave energy* in the artery, and taking no account of the *current energy*. The author, however, believes such a criticism to be entirely unwarranted. For, if we measure the wave energy in a peripherally closed artery, we are really measuring the entire energy from the heart exhibited at that

point, because the current at the periphery through the capillaries, which determines the amount of the circulation, is entirely due to this wave energy. The pressure in the capillaries arises wholly from the change of kinetic wave energy into potential pressure energy. This is illustrated by a fact easily shown by the sphygmograph. If even a single pulse be lost, the minimal pressure, *i. e.*, the base of the curve, instantly falls. The arterial pulse is therefore to be conceived as a kind of peripheral heart, working not automatically, to be sure, but by its elasticity, or, to a certain extent, by its resiliency. This conception of the pulse is set forth and defended in the author's work on the absolute sphygmogram. He considers it a most important one, and exceedingly fruitful in any study of the dynamics of the circulation. It at once makes clear the significance of sphygmobolometry.

If one assume, then, that by the sphygmobolometer he measures an approximately constant fraction of the entire heart energy (its exact value depending upon the constant of the instrument), it is possible to get at least approximately relative values for the active circulation.

Let W = the work done in the systole; P = the normal mean pressure in the brachial artery or the aorta; P^1 = the corresponding pressure in a pathologic case; S = the volume of the normal systole; S^1 = the volume of the abnormal systole. Then approximately:[1]

$$W = SP \quad \therefore \quad S = \frac{W}{P}$$

and

$$W^1 = S^1P^1 \quad \therefore \quad S^1 = \frac{W^1}{P^1}$$

$$\therefore \quad \frac{S^1}{S} = \frac{W^1P}{WP^1}.$$

Let $\frac{W}{n} = w$ represent that fraction of the entire work of the heart measured at the brachial artery by the sphygmobolometer in the normal case,

and $\frac{W^1}{n} = w^1$ in the abnormal case;

then $$\frac{S^1}{S} = \frac{W^1}{W} \cdot \frac{P}{P^1} = \frac{w^1n}{wn} \cdot \frac{P}{P^1} = \frac{P}{w} \cdot \frac{w^1}{P^1}$$

i. e., the systolic volumes vary directly as the amounts of work done (measured by the sphygmobolometer), and inversely as the corresponding mean arterial pressure.

If, now, the fraction $\frac{P}{w}$ be established once for all for normal cases, and be designated by N (normal), then:

$$(2) \quad \frac{S^1}{S} = N\frac{w^1}{P^1};$$

i. e., the ratio of the pathologic systole to a normal systole is equal to the product of the value N (including the constant of the instrument) by the ratio of the sphygmobolometric energy to the mean pressure in the pathologic case.

Of course, in a valvular insufficiency, only the utilized portion

[1] Sahli, Deut. med. Woch., 1907, No. 16.

of the systole is included in this computation because the unutilized portion of the systole, the regurgitation, does not appear in the sphygmobologram.

It is obvious that the foregoing conclusions will not hold unless the energy measured at the brachial artery represents a constant fraction of the entire heart energy (*i. e.*, N is a constant). It is, however, probable that such is the case, owing to the conditions of the procedure: (1) the brachial artery is converted into a blind appendage of the aorta; (2) it is, therefore, strongly distended; (3) the veins are cut off by the pressure in the cuff, and the capillaries therefore pulsate with the artery. Hence the conditions are in a great measure independent of the variations in caliber and contraction of the brachial artery, and, so far as this is possible in biologic questions, investigations on the work done by a single artery may also be used for comparative conclusions concerning the entire work done by the heart. This is all the more the case, since the influence of the state of contraction of the pulsating artery will be in a measure eliminated because of the relaxation of the arterial wall caused by the pressure of the cuff, and the best possible transmission of the pulse will thereby be obtained.

It must be emphasized that we do not measure the actual systolic volume in cubic centimeters. To do this we should be obliged to know the absolute value of the normal systole (S). We are able merely to measure the ratio between the volumes in circulation in the two cases. In other words, to decide whether in a given case the systolic volume is subnormal, normal, or above normal, and whether it remains constant during the period of observation, or increases, or decreases. These are the questions which sphygmobolometry can answer, and they are certainly most important questions for the practising physician. Time and clinical experience must, however, prove whether this new method of the author's is practically useful. It may at any rate be asserted that the technic is simple and requires but little time, not nearly so much as that needed for sphygmography and the graphic measurement of the maximum and minimum pressures, as determined by Janeway, Masing, Strassburger, von Recklinghausen, and Sahli. The first task must be to determine the normal figures for the cardiac energy exhibited in the arm by normal individuals of different heights and weights, with which to compare the results in pathologic cases. In passing it may be said that the effect of drugs on the circulation may be determined much more certainly by sphygmobolometry than by any other hydraulic method. The author will also here repeat what he mentioned in 1901 at the Berlin Congress for Internal Medicine, that an improvement of the circulation often results in no increase of arterial pressure, but that, paradoxically, the pressure is sometimes lowered. Therefore, as he has shown in his article on the absolute sphygmogram,[1] no conclusions concerning the condition of the circulation can be drawn from the maximum blood-pressure or even from the height of the absolute sphygmogram or the pulse pressure. But the sphygmobolometer curve distinctly shows any change in the circulation. See the curve showing the effect of digitalis, reproduced in the author's original article.

Sphygmobolometry cannot be replaced by the sphygmograph, although it is true in a way that it is the pulse energy that sets the sphyg-

[1] Deut. Arch. f. klin. Med. 1904, vol. lxxxi.

mograph in motion. For measuring the energy, sphygmobolometry has the following advantages over sphygmography: (1) the pulse of the whole extremity is being investigated in the neighborhood of the aorta, and not merely the pulse of one small artery; (2) the energy is transmitted permanently to the registering apparatus and is, therefore, independent of accidents of application and the caliber of the individual artery; (3) a simple formula is deducible instead of an exceedingly complicated empirical law.

It should be added that this procedure corresponds to the old-fashioned method of feeling the pulse, which sought to estimate the force of the pulse-wave rather than the height of the blood-pressure. This method has been entirely neglected of late on account of the disproportionate modern insistence on the static conception of the circulation, and yet this method of feeling the pulse ("energetisches Pulsfühlen") is perhaps the most practically useful one, since it focuses the attention on the work done by the pulse-wave without regard to the blood-pressure. (See p. 118 for the author's argument in its favor.) It *appreciates* the pulse energy, which the more exact methods of bolometry records and measures. It is obvious that the mere observation of the extent of the mercury excursions may be employed in diagnosis to show the size or, according to Marey, the strength [1] of the pulse. For clinical demonstrations the float should carry a paper flag to make its movements more easily visible at a distance. The author has already shown (p. 141) that in the ordinary sphygmogram the volume of the pulse has a very indefinite significance; but in the sphygmobologram it always represents a fixed amount of energy. In the interpretation of the results we must evidently beware of confusing the idea of "performances" (work accomplished) with "capacity for performances." (functional capacity).

This method measures, not the amount of work which the heart is capable of performing under increased demand, but the amount which it actually performs at a given moment, *e. g.*, the performance of the heart and the size of the circulation in a healthy individual at rest may appear very small; and yet this does not preclude such a heart's capacity for a very much greater task under the stimulus of vigorous muscular work. Hence in a given case the functional examination may have to be supplemented in this respect by noting the alteration of the sphygmobologram after making an increased demand of the heart, *e. g.*, lifting a weight with the free arm. With a heart capable potentially the work (W) (measured sphygmobolometrically) increases materially; with serious cardiac insufficiency, on the contrary, this work does not increase and may even decrease.

[1] In judging the cardiac energy, not only the extent of the mercury excursions, but also the overpressure, must be taken into account; and for judging the systolic volume the mean arterial pressure (see formula 1 (p. 185), and 2 (p. 187)). The latter formula shows that a high blood-pressure must be associated with a higher volume for the pulse energy than a low pressure if a normal systole is to be assumed. This also applies to the author's "energetic feeling" of the pulse.

VISIBLE PHENOMENA OF MOTION IN THE VESSELS

CAPILLARY PULSE

Under normal conditions the blood flows smoothly and without a pulse in the capillaries, either because the resistance in the smallest arteries completely deprives the pulse-wave of its energy at this point, or because, as von Frey and Krehl believe, the pulse-wave is completely reflected centripetally. (See p. 133 et seq.) Under some conditions however, the pulse is transmitted to the capillaries, and becomes evident to inspection in the form of a pulsating reddening and blanching of the parts in question. Whatever facilitates the entrance of a pulse-wave into the capillary areas, or whatever renders the flow into the veins difficult, will, of course, favor the production of a capillary pulse. The larger the pulse-wave and the more it approaches the type of *pulsus celer*, the more the conditions for a capillary pulse are favored. A capillary pulse is sometimes observed over hyperemic, and especially over inflammatory, areas, *e. g.*, over felons. Very frequently the patient himself appreciates the increased pulsation in inflammatory parts as a throbbing pain. The capillary pulse, due to a *pulsus celer*, especially in aortic insufficiency, is of far greater interest. This is a very common, although not a constant, sign in this valvular lesion. It is perhaps best appreciated by observing the alternate blushing and pallor at the finger-nail. Sometimes enough pressure upon the anterior part of the nail-bed to blanch the nail brings out a margin between red and white which oscillates with systole. Care should be taken not to allow the influence of the examiner's own pulse to cause a rhythmic pressure. The capillary pulse in aortic insufficiency may be very frequently appreciated at other places which are characterized by their redness, *e. g.*, ears, lips, cheeks.

[A clean glass slide lightly pressed upon the extended lower lip will sometimes bring out the capillary pulse when it cannot be appreciated at the finger-nail. Another useful device is to rub a spot upon the forehead until it is hyperemic and then look for an alternation of redness and pallor.—Ed.]

Contrary to many statements, a capillary pulse is by no means pathognomonic of aortic insufficiency. Any condition which will produce a *pulsus celer* (exophthalmic goiter, fever, chlorosis) will be apt to show a capillary pulse. If the circulation be very active, it may sometimes be observed even in health. Although not absolutely pathognomonic of aortic insufficiency, it is so common in this lesion and so rare in other conditions that the sign really possesses considerable diagnostic significance. The sign becomes most distinct during the stage of compensation. The existence of an actual stenosis complicating the insufficiency may interfere with the appearance of a capillary pulse. The retinal vessels will show a visible pulsation with the ophthalmoscope when a capillary pulse is visible elsewhere.

THE EFFECT OF RESPIRATION UPON THE VEINS

The respiratory variations in the interior of the thorax, as is well known, influence the venous circulation very distinctly. Inspiration

hastens, expiration retards, the flow of venous blood. The influence is ordinarily not evident in the visible veins with superficial breathing,

Fig. 106.—Venous engorgement during forced expiration—case of phthisis (New York City Hospital).

Fig. 107.—Distention of jugular vein, accentuated during inspiration; a case of leukemia with enlarged mediastinal glands (Dr. Joseph Collins, New York City Hospital).

but forced breathing will produce an inspiratory diminution and expiratory increase in the size of these veins, and if they be already dis-

tended by congestion, the change will become still more evident. Both conditions are usually present in dyspnea.

Variations in intrathoracic pressure become more distinct during coughing or other exertions which raise the abdominal pressure. The intrathoracic pressure then becomes markedly positive, and the veins, especially the cervical veins, become decidedly distended during the coughing paroxysm or effort of straining, while during the next deep inspiration they suddenly collapse again. When this periodic congestion is frequently repeated, especially in patients who suffer from chronic cough, a permanent dilatation of the veins, particularly of the jugular, may result, so that with coughing or straining the whole lower portion of the neck becomes swollen. The "bulbs" of the jugular veins may appear as large swellings, either just inside or outside of the insertion of the sternocleidomastoid (Fig. 106). The bulging of the supraclavicular fossæ during a cough, therefore, should not always be attributed to a distention of the lung apices (p. 107.)

In very rare cases the reverse condition is observed, *i. e.*, a distention of the veins during inspiration and a collapsing or a diminution during expiration; this always suggests that during inspiration some mechanical compression of the veins exists within the chest. This phenomenon has been described as a sign of fibrous mediastinitis, like the pulsus paradoxus. (See p. 142.) It may, however, depend upon the effect of inspiratory pressure or traction upon the large veins leading to the heart, due to interference with the mobility of the thoracic contents (pericarditis, pleuritis, mediastinal tumors, see Fig. 107).

THE VENOUS PULSE

The arterial pulse-wave usually disappears in the capillaries, *i. e.*, it is reflected centripetally (see p. 190 et seq.), so that the blood no longer pulsates, but flows uniformly in the venous radicles. Nevertheless under both physiologic and pathologic conditions characteristic pulsations synchronous with cardiac action are frequently observed in the greater veins lying near the chest (almost exclusively in the jugular veins).

There are several pathologic varieties of this pulsation. One type of venous pulse must, however, be considered absolutely physiologic, because it is constantly observed after exposing the vein in healthy animals, and because individuals who show it are perfectly normal. That this venous pulse is not observed in everybody is due to the fact that in some people the jugular veins are not visible or are seen only with considerable difficulty. Conversely, this physiologic venous pulse can naturally be seen with especial readiness in people whose veins have become more noticeably distended by congestion.

If the valves at the upper end of the jugular bulb close properly, the venous pulse will be chiefly apparent in the bulb (bulbous pulse). The closure of the bulbous valves prevents only the actual regurgitation of blood as it occurs in the venous pulse of tricuspid insufficiency, and not its wave-like motion coming from the heart. The latter, in closing the bulb valves, produces above them, from the backing up, a positive wave of exactly the same shape. Consequently, by carefully watching a bulbous pulse, we can appreciate that the veins do pulsate above the bulb valves, although less than below. Very

frequently, however, as the result of congestion, the venous valves become insufficient, so that the pulse may be seen just as distinctly in the upper part and in the small branches of the jugular vein as over the bulb itself.

When the distended veins become distinctly visible (in venous pulse the external jugular veins are chiefly concerned), it is generally a simple matter to distinguish between their pulsation and that of the neighboring arteries. The pulsation of some deeply seated vein (internal jugular) which cannot be directly observed is much more difficult to determine. But even then the venous pulse can be easily recognized, particularly by the large area of pulsation involved, corresponding to the large size of the vein, by the slow, undulating transmission of the beat, and by the very moderate amount of power to be felt in the pulsation, depending upon the slight amount of tension of the venous contents. If the pulsation be transmitted from an artery to a vein, compression of the vein will not affect the pulsation peripheral to the point of compression, and sometimes the resulting congestion will make the pulsation even more distinct. An accentuation of the pulsation from compression otherwise occurs only with the very rare penetrating venous pulse. (See p. 197.) Under some circumstances the venous pulse may also be appreciated at the liver as the liver venous pulse.

A reliable diagnostic valuation of the venous pulse and a sure differentiation of its varieties can only be obtained by comparing its phase and rhythm with the

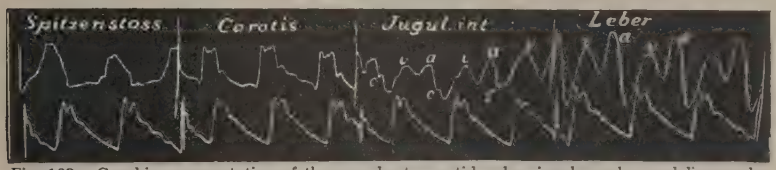


Fig. 108.—Graphic representation of the apex-beat, carotid pulse, jugular pulse, and liver pulse compared with the radial pulse (after Mackenzie).

phase of the heart action and the rhythm of the arterial pulse. Since this determination by mere inspection and palpation is very difficult, it is best to make use of the graphic method, whereby both pulses can be recorded.

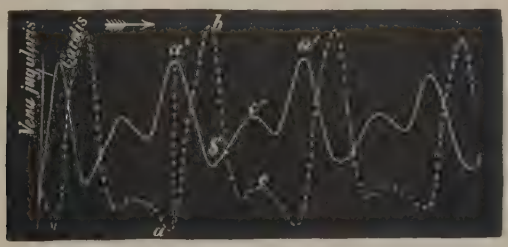


Fig. 109.—Physiologic (negative, presystolic) venous pulse (Riegel).

An easier procedure has been advocated by Volhard.[1] By means of small glass funnels, one of which is placed over the pulsating vein or over the liver area and the other over the carotid, the pulses are transmitted through hollow tubes to two manometers filled with differently colored fluids and placed side by side. It

[1] Congress for Internal Medicine, 1902.

is then very easy to ascertain whether the two water columns rise alternately or simultaneously. On account of their inertia the two columns of water should be of the same height. The connecting tubes, however, need not be of equal lengths, because the air-waves are propagated through them with the velocity of sound.

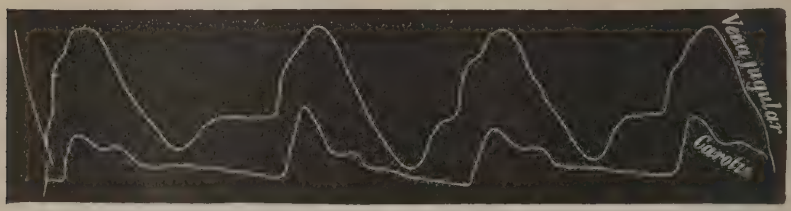


Fig. 110.—Positive centrifugal (systolic) venous pulse in tricuspid insufficiency (Riegel).

This procedure sometimes gives very definite results, but sometimes fails on account of the difficulty of fully isolating the venous pulse from the movement imparted to the vein by the carotid. The same difficulty is met in the graphic method (see below).

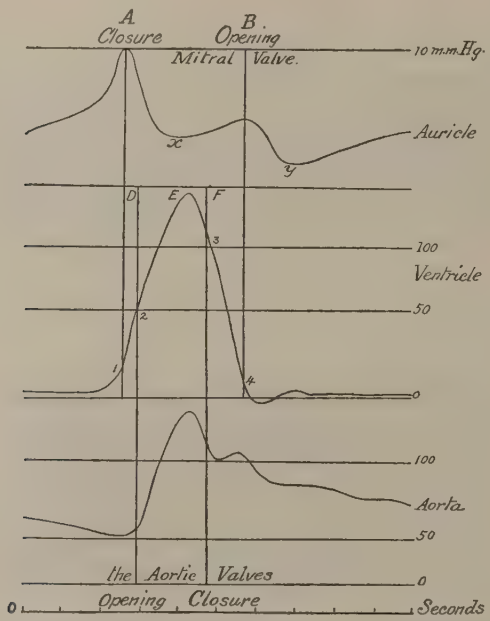


Fig. 111.—Diagrammatic representation of the course of the pressure during one heart cycle in the auricle, ventricle, and aorta (after von Frey).

For the graphic method we usually select the external and internal jugular veins and the radial artery. The apparatus is described on p. 126 et seq. Simple glass funnels, or the metal receivers used by Mackenzie (Fig. 129), are placed on the artery and on the vein. On the latter, a spot as free as possible from the trans-

mitted arterial movement, should be selected. The two curves are recorded on the same paper (Mackenzie). In spite of the fact that the radial pulse is delayed in relation to the apex-beat by the length of closure time, and by the time necessary for transmission of the pulse to the artery, it is usually easy to decide whether the venous pulse is synchronous or alternate, with the ventricular systole. If any difficulty is experienced, it is advantageous, as Mackenzie has shown (see p. 152), to compare the radial pulse with the apex-beat, carotid pulse, and venous pulse in succession, as in Fig. 108 (Mackenzie).

The jugular venous pulse is generally more distinct if the patient be recumbent. We cannot always interpret every peculiarity of such a venous pulse-curve, because the arterial pulse often inevitably interferes with the venous pulse, and sometimes secondary peaks are caused by reflected waves, which cannot be properly explained, and which may lead to erroneous and arbitrary conclusions.

Until recently two varieties of the venous pulse were sharply differentiated as follows: *a*, Fig. 109, which represents the so-called "physiologic venous pulse," "negative venous pulse," "systolic venous collapse," "venous undulations," "negative centrifugal venous pulse," or "presystolic venous pulse"; and *b*, Fig. 110, which represents the "pathologic," "positive centrifugal," or "systolic" venous pulse. This sharp distinction, and with it a part of the nomenclature, must to-day, however, be abandoned, as is evident from the following discussion of the origin and essential nature of the venous pulse.

The venous pulse is plainly due to rhythmic variations in the pressure of the venous blood. Except in one instance, to be discussed later as the "penetrating venous pulse" (see p. 197), the rhythmic movement of the arterial blood has been lost before it reaches the veins, so that the variations of pressure in the ordinary forms of the venous pulse must be due to impulses starting from the right auricle and transmitted against the blood-current. The study of the variations of pressure in the right auricle, under physiologic and pathologic conditions, must, therefore, furnish the key to the explanations of the venous pulse. Von Frey's[1] exact analysis of the variations of pressure in the auricle, ventricle, and aorta is represented in the following diagram:

The classification of the venous pulse attempted here is supported by the following discussion.

AURICULAR VENOUS PULSE

The pressure-curve of the normal auricle must evidently represent, with but insignificant variations, the normal venous pulse-curve. (Compare Fig. 109, the physiologic venous pulse, with the upper curve in Fig. 111.) The obliquely ascending line with which the curve begins (Fig. 111) is the expression of the filling of the right heart by the continuous influx of blood from the veins, and is modified by the increased intrathoracic pressure caused by the increase in the size of the heart (auxocardia), which diminishes the suction and tends to produce stasis in the veins. The steep rise following it is the effect of the systole of the right auricle by which, since the pressure works equally forward and backward from the auricle, the pressure in the veins is increased in spite of the emptying of the auricle into the right ventricle. It is by no means necessary to assume an actual regurgitation of the blood into the veins. Physiologists assume that this is prevented by the circular contraction at the venous orifices coinciding with or even before the auricular systole. The damming of the venous stream by the increased pressure in the auricle, plus this contraction, produces a stasis wave in the veins. The apex of the venous curve, and that of the auricular curve, correspond then to the systole of the auricle (presystolic). During the diastole of the auricle, corresponding to systole of the ventricle (Fig. 111), the auricular pressure falls and the curve descends rapidly to *x*. This steep auricular descent, the most strongly marked characteristic of the so-called normal venous pulse, is apparently also due in part to the negative pressure in the thoracic cavity, caused by the lessening of the volume of the heart during systole (meiocardia) which sucks the venous blood toward the heart. For, as the figure shows, the fall of the venous pulse-curve coincides with the aortic pulse, *i. e.*, the period of meiocardia. From the point *x* the pressure in the auricle and veins rises again, because the relaxed auricle is again being filled. In the first part of this period the ventricle is still contracting. At the moment when ventricular diastole begins (line 4 in Fig. 111) the auriculoventricular valves open, and the pressure naturally sinks again in the auricle and veins, the curve falling to *y*. This completes one heart cycle and one so-called normal or physiologic venous pulse. Since the summit corresponds to the systole of the auricle, the terms *presystolic* and *auricular*

[1] Die Untersuchung des Pulses, Berlin, 1892.

venous pulse are both justifiable, as is also the term *physiologic*, in so far as this pulse is to be observed under quite normal conditions, provided the veins are plainly visible. The expression "negative" pulse should be abandoned, for it puts too great emphasis on the depression of the auricular curve (x, Fig. 111), which is called a negative wave, as if any such negative wave or fall were possible without a preceding positive wave or rise. This explanation of the venous pulse is in no way affected if one assume an actual regurgitation of blood into the veins instead of mere stasis on account of the hindrance to the blood-stream, for either cause would give rise to a positive centrifugal venous wave. Mackenzie's designation of the second apex (between x and y, Fig. 111; c', Fig. 109), as the *ventricular* wave is not justifiable, because this summit is not the expression of the ventricular contractions as the first summit is of the auricular contraction, but occurs only after the greater portion of the ventricular contraction is finished. The fact that the depression y is due to the relaxation of the ventricle is not sufficient to justify designating the summit B as the ventricular wave. Under pathologic conditions, to be sure, a truê ventricular wave may be developed from this second summit, as we shall see below, and this is evidently responsible for Mackenzie's incorrect terminology.

VENTRICULAR VENOUS PULSE WITHOUT TRICUSPID INSUFFICIENCY

The normal venous pulse may be altered by either one of two conditions: (1) Paralysis of the auricle, often caused in heart disease, as Mackenzie has shown, by the distention of the walls from stasis; and (2) tricuspid insufficiency.

In the former the auricular wave, which is characteristic of the physiologic venous pulse, obviously disappears more and more completely. The factors which then cause alterations of pressure in the auricle and veins are: (1) The gradual passive increase of pressure, resulting from the augmented filling of auricle and ventricle together with the increasing intrathoracic pressure (auxocardia); (2) the contraction of the right ventricle, causing stasis in the veins and right auricle; and (3) the diastole of the right ventricle, suddenly unloading the auricle. The negative intrathoracic pressure (meiocardia), dependent upon the systolic emptying of the heart, tends to suck the blood from the veins, to be sure, and so opposes the stasis due to ventricular contraction, but its effect upon the veins is less direct and rapid, so that it cannot prevent the stasis. Neither can the increased intrathoracic pressure (auxocardia) overbalance the stronger suction of the ventricular diastole. The two important factors, then, are: (1) The systole of the right ventricle, causing stasis; and (2) the diastole of the right ventricle, unloading the auricle and veins. The resulting venous pulse will be synchronous with ventricular systole, and may, therefore, be called a *ventricular systolic venous pulse.* Its form is shown in Fig. 90, although there it is due to the regurgitation of the blood in tricuspid insufficiency, and not to paralysis of the auricle. (See Fig. 110.) It is obvious that different degrees of insufficiency in the muscle-wall of the auricle will give rise to differing transitional forms between the physiologic auricular pulse and the purely ventricular pulse of paralysis of the auricle (Fig. 112), and that, as the wave A (Fig. 111) grows smaller the wave B will be shifted backward into the point corresponding to that of ventricular systole.

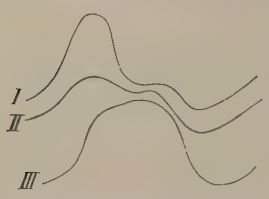


Fig. 112.—Diagram showing the transformation of the auricular venous pulse (*I*) by gradual disappearance of the auricular wave into the ventricular venous pulse (*III*) caused by increasing paralysis of the auricle without tricuspid insufficiency.

VENTRICULAR VENOUS PULSE RESULTING FROM TRICUSPID INSUFFICIENCY

In this case the regurgitation of the blood during the systole of the right ventricle causes a venous pulse of ventricular systolic type. Unless the auricle has lost its ability to contract, the physiologic, presystolic, or auricular pulse will also show more or less plainly. The more the distention of the auricle paralyzes its wall, the less prominent the auricular wave appears. In Fig. 110 it is still visible as an anacrotic elevation. An increase of the tricuspid insufficiency, accentuating the steepness of the ventricular wave's ascending limb, anticipates its summit, and so conceals the auricular wave. A comparison of such a venous pulse with the carotid pulse (Fig. 110) shows that the former occurs slightly before the latter. This may

be due to the fact that the first portion of the ascending limb of the venous pulse-curve is still due in part to the auricular contraction, but it can also be explained by the fact that the regurgitation toward the veins coincides with the beginning of the ventricular contraction, while the aortic valves do not open until the pressure has augmented, *i. e.*, at the end of the so-called "closure time," a term, to be sure, only partially applicable in tricuspid insufficiency. On account of its greater energy this variety of venous pulse is the one which most readily gives rise to an audible tone at the bulbous valves of the jugular vein. (See Auscultation of the Veins.)

TRANSITION FORMS BETWEEN THE AURICULAR AND THE VENTRICULAR VENOUS PULSE; THE CAROTID WAVE

Such forms are due most frequently to the varying degrees of completeness of the auricular contraction (see above), but angular venous pulse-waves are also sometimes due to the influence of the carotid pulse, manifesting itself either in a dislocation of the whole venous curve or as a peculiar extra elevation in the curve (Fig. 113).

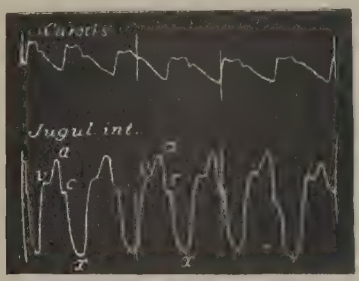


Fig. 113.—Physiologic (so-called auricular) venous pulse with an extra elevation (*c*) arising from the carotid pulse (after Mackenzie). As the figure shows, *c* is synchronous with the carotid pulse; *v* is Mackenzie's so-called ventricular wave (p. 196).

The latter may be seen more plainly on deep inspiration. The recognition of such variations is essential to the proper understanding of many modifications of the venous pulse, although they cannot be given a simple name.

POSITIVE CENTRIPETAL OR PENETRATING VENOUS PULSE

This rare type of venous pulse is produced when the arterial wave possesses sufficient force to penetrate the capillaries and transmit a pulsating motion to the venous radicles. It is illustrated in the experiments of Claude Bernard, who, by stimulation of the chorda tympani, dilated the vessels of the submaxillary gland sufficiently to cause the arterial pulse to be transmitted to the veins. The phenomenon evidently depends upon conditions similar to those producing the capillary pulse and has been found chiefly in aortic insufficiency. Quincke, however, believes that a capillary pulse does not always accompany a penetrating venous pulse, but, on the contrary, that we may be unable to appreciate the pulse-wave in the capillaries because it is spread over too great an area, whereas the decrease of the sectional area of the streams in the venous radicles, under favorable pressure conditions, may cause the pulse to become visible again. This type of venous pulse occurs especially with an arterial pulsus celer; perhaps also in pronounced hyperemia of the tissues with excessive dilatation of the capillaries. It usually appears, not in the jugular vein, but in the small veins of the extremities. Compression will obliterate the pulse in the central portion, but not in the peripheral part of the vein.

DIASTOLIC VENOUS COLLAPSE (FRIEDREICH)

This very rare phenomenon was described by Friedreich in connection with systolic retraction from pericardial adhesions. (See later Palpation and Inspection of the Precordia.) The diastolic bulging of the chest-wall produces a diastolic suction within the thorax, and this is supposed to cause the veins to collapse. It is,

so to speak, the reverse of the physiologic auricular venous pulse. In the latter the vein is flattened during systole; in the phenomenon described by Friedreich the collapse occurs during diastole. It is, therefore, somewhat similar to the ventricular venous pulse. According to Brauer's theory of the diastolic thoracic projection, the diastolic venous collapse would be considered as a direct result of an accentuated diastole.

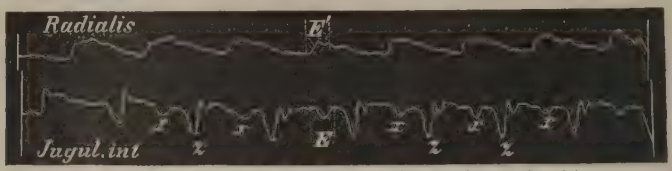


Fig. 114.—Friedreich's diastolic venous collapse (after Mackenzie).

The diastolic venous collapse may be differentiated from the ventricular venous pulse by the visible thoracic diastolic projection, and chiefly, according to Mackenzie, by the broad plateaus in the curve between the diastolic depressions (Fig. 114).

THE LIVER PULSE

A pulse palpable at the liver is generally the expression of a venous pulse demonstrable also at the jugular vein. But an *arterial liver pulse* may occur with a pronounced pulsus celer of aortic insufficiency and in inflammatory conditions of the liver. The *liver pulse* can be appreciated best by palpating the liver, as far as possible to the right of the median line, so as to avoid confusion with an epigastric pulsation or with an aortic pulsation, which is sometimes transmitted to the liver. (See later section upon Palpation and Inspection of the Precordia.) To avoid such errors, it is especially important to be convinced that the pulsation is really expansile, *i. e.*, that the volume of the liver increases intermittently. This can generally be best accomplished by firmly grasping the edge of the liver, or by employing bimanual palpation, one hand behind pressing the liver forward against the other hand in front. This is usually easy on account of the enlargement of the organ.

For the graphic record of the liver pulse, Mackenzie's "liver receiver" (p. 129) is pressed closely around the edge of the organ and the side opening then closed with the finger. The pulse is then recorded in the same way as the venous pulse at the jugular vein.

It was formerly held that a plainly expansile liver pulse was always systolic (ventricular), and, if an arterial pulse were excluded, it was a reliable diagnostic sign of tricuspid insufficiency. But Volhard has shown that in congestion of the liver, a presystolic (auricular) pulse is not infrequent. The author's theory of the venous pulse in general would also militate against even the systolic liver pulse being conclusive evidence of tricuspid insufficiency. (See p. 195.)

Mackenzie reports that in congestion of the liver he has practically never failed to demonstrate a liver pulse graphically, and that it is a much more constant symptom than a jugular venous pulse. This may be easily explained by the fact that the stasis is much more marked at the liver, because at the neck it is combated by the force of gravity, tending to empty the veins.

In opposition to Volhard, Mackenzie considers a presystolic liver pulse a sign characteristic of tricuspid stenosis.

Mackenzie has shown that epigastric pulsations may shove the liver outward during systole corresponding to the negative character (the systolic retraction) of the ordinary epigastric pulsation assumed by him. This movement of the liver will give rise to a curve like that of a presystolic auricular venous pulse, except that the wave *B* (Fig. 111) will be lacking. In such cases the differential diagnosis may be made by means of palpation.

An *arterial liver pulse*, as has been said, sometimes occurs in aortic insufficiency as a result of the pulsus celer and in inflammation of the liver. It can be differentiated from the *venous liver pulse* only by a careful consideration of all other conditions.

REMARKS ON THE MODERN UTILIZATION OF THE VENOUS PULSE-CURVES FOR THE ANALYSIS OF DISTURBANCES OF THE RHYTHM OF THE HEART-ACTION

In the recent literature on the rhythm of the heart action and its disturbances, many attempts have been made to deduce, from the graphic records of the venous pulse, far-reaching conclusions concerning the nature of the action of the right heart, and so to obtain data for the interpretation of any anomalies of the heart action present. The author considers these attempts proper and praiseworthy, but lacking in sufficient searching criticism on the part of those presenting them. The latter have not taken into account the enormous difficulty, especially in irregular pulses, caused by reflected waves. Just as in the arterial pulse-wave, the primary wave is often confused by all kinds of secondary reflected waves, of whose diagnostic significance we know but little (see p. 133) on account of their involved etiology. The same difficulty occurs with the venous curve, and the detection and interpretation of secondary waves in the latter is even more difficult. For, on account of (1) the low pressure; (2) the marked variations in pressure with different positions of the body caused by gravity; and (3) the slow rate of propagation of the wave, whose movement may often be followed with the eye, the retardation of the reflected waves, and consequently their position in the curve, are much more variable than in the arterial pulse-curve. The carotid pulse may also interfere with and influence the venous curve in varying ways, depending on its own form and on the place at which it acts upon the vein. The influence of respiration has also been too little considered. In irregular heart action, where, to be sure, these analyses of the venous pulse play an important part, the difficulties of such analyses become often immeasurable, just on account of the irregularity and the persistent variation with each heart action. (See p. 152 et seq.). The positiveness with which such problematic interpretations of highly irregular venous pulse-curves have been presented in recent writings is very astonishing, and evidently comparable to the phase in the history of the arterial sphygmogram, now past, when from it, too, were drawn similar far too extensive conclusions.

PERCUSSION

PERCUSSION IN GENERAL: INSTRUMENTS

The examination of the human body by means of percussion (or striking) plays an especially important rôle in the modern diagnostic methods of internal medicine. The condition of the organ or organs underlying the spot percussed is determined or, at least, inferred from the sound produced. We accredit the discovery of this method to the Vienna physician Auenbrugger, for in the year 1761 a description of it appeared in his work, *Inventum Novum*. However, the method was not generally employed until after Corvisart, Napoleon I.'s, physician, translated Auenbrugger's work into the French (1808) and appended extensive observations of his own as commentaries. Manifold modifications, theoretic confirmations, and improvements in interpretation were then added to the method by a great number of authors, of whom we need only mention Piorry, the inventor of the pleximeter; Barry, the inventor of the percussion hammer; Wintrich, Skoda, Traube, and A. Geigel. Hence, although the method is already more than a century old, it really only became the common property of physicians during the second half of the nineteenth century. To-day percussion and auscultation have become the corner-stone of diagnosis. The student must learn both at the very beginning of his clinical experience.

There are countless methods of percussion. Originally only *imme-*

diate (*direct*) *percussion* was employed, *i. e.*, the striking of the surface of the body directly with the tips of the fingers. But where the body-covering is soft, such a method will elicit only indistinct and impure sounds, and therefore to-day we use almost exclusively *mediate* (*indirect*) *percussion*, *i. e.*, either a finger of the other hand or a specially constructed instrument—the pleximeter—is interposed between the striking finger and the surface of the body. The theory of this arrangement has been recently worked out by R. Geigel.[1] The "plexor" is a small hammer furnished with a rubber tip. It may be substituted for the striking finger.

In *mediate* (*indirect*) *percussion* we may use either: (1) Finger-finger percussion; (2) finger-pleximeter percussion; or (3) plexor-pleximeter percussion.

Individual taste or habit will generally determine a preference for one of these methods. There are certain differences and advantages in each, although we may be skilful or awkward with any one of them. The finger-finger percussion is the most difficult to learn; but in many cases it furnishes more accurate results than the pleximeter percussion, because the inherent note of the pleximeter is liable to confuse the percussion tone. It has been held by many authors, particularly by Ebstein, that, consciously or unconsciously, the sense of touch in the finger-finger percussion aids the sense of hearing (palpation-percussion).[2] But the chief advantage is that the physician is independent of instruments, which may be readily forgotten, mislaid, or broken. The finger pleximeter, and especially the plexor-pleximeter, percussion methods are much easier to learn, and greater differences of sound may be more readily demonstrated and appreciated by a larger circle of listeners; nevertheless, a percussion-note which is loud enough to be heard at considerable distance is suitable only for certain cases (see below). A physician should be familiar with all three methods, and he should be able to control his own results by applying first one and then the other, for despite the utmost care and great skill, the subjective har-

[1] Deut. Arch. f. klin. Med., 1907, vol. lxxxviii, p. 598.

[2] This conclusion has recently been combated by Moritz. He maintains that if all aid from the sense of hearing be excluded (by closing the ears and working in a noisy room) the sense of touch alone will lead to either negative or erroneous conclusions. He is, therefore, inclined to consider that the sensation of a greater or less resistance appreciated by the touch, which indisputably accompanies the acoustic perception on percussion, is in reality only a secondary sensation. It is to be considered as suggested by the sensations, appreciated by the hearing, or as the result of an unconscious process of induction. In other words, one reasons from a loud percussion-note to a less resistance, from a faint note to a greater resistance. The author shares these misgivings. He is also inclined in general to condemn the combination of two kinds of sense impressions in one method of examination. If he wishes to palpate, he palpates, and uses no accompanying percussion. If he is percussing, he considers it best to concentrate his entire attention on the sounds heard, which often are appreciated exactly and correctly judged only with difficulty. In any case, this mixing of sense impressions contains an instinctive, almost an unconscious, element, which offers great difficulties for scientific analysis and for teaching purposes. The beginner cannot easily be shown how to direct his attention in percussion toward two sensations at once, both of them, moreover, difficult to appreciate and to judge. A certain mastery of the procedure, gained by long experience, is essential. Ebstein especially recommends his palpation percussion for the determination of the total size of the heart (corresponding to the deep cardiac dulness). But it is difficult for the author to understand how such deep-lying boundaries can be appreciated by touch. He would consider that the palpatory sensations in that case would be determined rather by the conditions of resistance of the thorax in the neighborhood of the heart, taking into account the sternum.

acter of the method often in difficult cases leaves a doubt in the mind of the examiner. A plexor and pleximeter are of some advantage in the employment of the plexor-pleximeter method (p. 205), although we can substitute a bit of wood, a pencil, or the like for the plexor, and a coin or another bit of wood for the pleximeter.

In certain cases (*e. g.*, for determining slight pathologic dulness in the chest or abdomen and for differentiating the deep cardiac dulness) *immediate (direct) percussion* is to be recommended as a control. The examiner thus avoids too strong pressure of the pleximeter or of the finger of the left hand, a very common fault with beginners. *Immediate (direct) percussion* is made by striking with the tip of the middle finger or the tips of the four fingers and thumb of the right hand arranged like a pyramid.[1] In percussing the lung apices beneath the clavicles the bone serves as a pleximeter, and the middle finger of the right hand as the plexor.

Laennec combined percussion and auscultation by listening with the stethoscope at a spot near to that being percussed ("percussion auscultation," "percussion transsonance," see the use of this principle in the "stick-pleximeter" percussion, p. 205). Runeberg has recently called attention again to this procedure, recommending its use in general in determining the boundaries of an organ. He places the stethoscope over the spot at which the organ in question lies nearest the thoracic wall. He then percusses over the organ lightly, if it lie deeply or merely strokes the skin with the finger if the organ lie superficially. The finger is then gradually moved away from the stethoscope. As long as it is over the organ, a distinct sound is heard, transmitted through the organ and the stethoscope apparently directly to the ear, but as soon as the boundary of the organ is passed, the sound disappears or loses its direct character. Runeberg claims that in this way he is able to map out both superficial and deep organs, and to distinguish not only, as in ordinary percussion, the boundaries between air-containing and solid organs, but also those between two air-containing or two solid organs (*e. g.*, stomach and colon, colon and small intestine, heart and liver, liver and gall-bladder, heart and a neighboring pleural exudate, air in the thorax and lungs or stomach). The author has not been able to confirm these results. He considers the method reliable only for the determination of the boundary between a solid and an air-containing organ, and then only when both lie superficially and when percussion, not stroking with the finger, is used, because if stroking be employed, the sound produced by friction with the skin is too prominent. The deeper the organ lies, the more subjective and unreliable he finds the method. He has failed entirely to determine by it the boundary between organs not differing in their air-content. He is, therefore, not convinced that it is better than ordinary percussion. Smith and others have announced very peculiar results in the diagnosis of heart conditions by their so-called "friction method," *i. e.*, listening with the "phonendoscope" (see section on Auscultation) to the sounds produced by friction against the skin. These investigations were undertaken chiefly in the interest of the total abstinence movement, and the results cannot be confirmed by objective observers. The author considers the method absolutely worthless and misleading.

Only continued practical experience can teach the technic of percussion, and but few rules are worth stating.

The percussion stroke should be made perpendicular to the surface of the part percussed.

The So-called "Orthopercussion."[2]—Goldscheider has recently recommended that in the percussion of the deep cardiac dulness the stroke should be made perpendicular to the frontal plane and not to the surface of the body, even when the sides of the thorax are being percussed. He claims that in this way "sagittal sound-waves" are dispersed through the thorax, and that, therefore, the true size of the heart is projected upon the thoracic wall, uninfluenced, as in perpendicular percussion, by the convexity of the surface of the thorax (comparable to Moritz's orthodiagraphy with Roentgen rays). The author finds two objections to this theory. In the first place, a body of such complicated form and structure as the thorax with its contents cannot possibly vibrate exclusively in one linear direction, or even

[1] Zeit. f. klin. Med., vol. xlii.
[2] Deut. med. Woch., 1907 (two numbers) and Cong. f. inn. Med., 1907.

predominantly so, as Goldscheider more cautiously puts it in the last-cited publication. The vibrations must be considered as curves of three dimensions, whose greatest axis depends not only on the direction of the stroke, but also on that of the axis of maximum elasticity. A second and much more important objection is the fact, that in percussing toward the sides of the thorax the direction of the blow would become more and more nearly tangential to the surface, and, therefore, a continually increasing part of the force would be ineffective in producing vibrations. In other words, the force of the percussion blow would be a variable not a constant. This method would, therefore, be approximately accurate, according to the author's experience, only for parts of the thorax lying nearly in the frontal plane, *e. g.*, in general for a heart of normal size. It would be difficult to make such a method apply to a heart whose apex-beat is felt in the axillary line. This is the cause of the dulness always elicited by percussion over a sharp convexity of the bowed ribs, for the reason that a larger proportion of percussion stroke impinges in the direction of the axis of the ribs and is lost in their arch.

In finger percussion the nail of the percussing finger should be cut short, and the blow should be struck with the pulp of the last phalanx in such a manner that not only the direction of the stroke but also the axis of the last phalanx is perpendicular to the pleximeter and to the surface of the body part percussed. A perpendicular stroke is essential for producing a good, uniform note. It is especially difficult for the beginner unless he be a piano player. Both in plexor and in finger percussion the stroke should be light, short, and elastic, produced by merely bending the wrist-joint, at the same time avoiding any cramped position of the hand or fingers. Percussion should in general be light (weak) (see later). Many beginners misinterpret the distinction between light and strong percussion, a mistake which should be avoided. (See p. 215.) The so-called *strong* or *deep percussion* should also in most cases be quite delicate, so that the note cannot be heard at any great distance.

The pleximeter, *i. e.*, the finger to be struck, should be placed with its palmar side upon and in close contact with the surface of the body and parallel to the border to be differentiated. Only light pressure should be employed, because strong pressure even with light (superficial) percussion will cause a diffuse vibration of the body on account of the larger area affected, and so simulate the effect of a stronger (deep) percussion. (See p. 213.)

Instead of the usual plexímeter, a bit of firm, gray erasing rubber, cut about 1 cm. wide, 1 cm. thick, and 4 cm. long, will answer the purpose well if the physician be not skilled in finger percussion. Like the finger, such a plexímeter has practically no intrinsic curve; it can be easily bent to conform to the curves of the chest-wall, and it can be struck with the hard end of the hammer or with the finger.

In percussing a child's body very much less force must be used than for the adult. (See Deep and Superficial Dulness.)

QUALITY OF THE PERCUSSION

RESONANT AND DULL, TYMPANITIC AND NON-TYMPANITIC, PERCUSSION-NOTES[1]

Even a layman, percussing different regions of the body surface, is able to recognize that one part furnishes a resonant, another part a dull, note. An accurate differentiation between resonant and dull notes, or between different grades of resonance, is the groundwork of percussion.

[1] For the theory of the origin of the different tones, see p 206.

A typically resonant note can be obtained by percussing over the lung; a typical flat note, by percussing over great muscle masses, *e. g.*, the thigh. Experience has taught us that resonant notes are produced over organs containing air; dull notes over organs without air, quite irrespective of whether they are solid or filled with fluid. Therefore percussion, on the one hand, defines the boundaries of the different organs; and, on the other hand, by changes in the resonance of the note, determines any increase or decrease of air contained in the organ. The less air, other conditions remaining the same, the duller the note. The resonance of the note also varies decidedly with the deep diameter of the air-containing organ, *i. e.*, the diameter in the direction of the percussion stroke. The thicker the layer of air, the more resonant the note. (See the section on Deep Dulness, p. 213.) The influence of the tension of the wall surrounding the air cavity upon the resonance of the note will be mentioned later.

We apply the terms *resonant* and *dulled* to the percussion-notes, using these words as they are ordinarily employed. *Clear* is often used as synonymous with *resonant*, and *muffled* as synonymous with *dulled*. But these terms should be abandoned, since in common usage *clear* usually implies a high, and *muffled* a low, tone, so that beginners may easily be led into misconceptions by their use. The word *dulled* as opposed to *resonant* is, on the contrary, unmistakable. When a resonant note is modified by a dulled note, we speak of the presence of *dulness;* a note which is neither very resonant nor very dull is called *relatively dulled;* an absolutely dull note, on the contrary, *absolutely dulled* or *flat*. The terms *absolute* and *relative dulness* have a corresponding signification.

In defining the quality of a percussion-note many modern authors employ the terms short and long as synonymous with dull and resonant. Theoretically, this is not quite correct, because the latter expressions characterize the intensity of the note; whereas short and long refer, on the contrary, to its duration, and the latter must depend upon the size and elasticity of the vibrating mass. The length of a musical instrument's note is of very essential importance to the tone and value of the instrument. A musical ear can, in fact, easily differentiate this peculiarity of duration in a percussion-note. However, in the relations of percussion which concern us a resonant note is almost always long and a dull note short. The exceptions to this rule have no special diagnostic importance, so that the expressions short and long may as well be eliminated.

There are countless gradations in quality between the two extremes resonant and flat or clear and muffled, the differences depending upon the amplitude of the note vibrations. There are, however, other very important differences of quality which we must heed and which depend upon variation in the form and number of vibrations. The most important of the latter is the distinction between *tympanitic* and *non-tympanitic* resonant notes. This distinction is illustrated by comparing in a healthy person the note obtained over the lung with that obtained over the air-containing abdominal viscera. The pulmonary note is resonant, but not tympanitic. The note over the stomach and intestines is resonant, and also tympanitic. Both tympanitic and non-tympanitic notes are really noises in the purely physical sense; but in tympanitic notes the vibrations are sufficiently periodic (*i. e.*, tuneful) for the ear to be able to compare their number with the number of vibrations of other sounds; in short, to be able to recognize a certain pitch. This

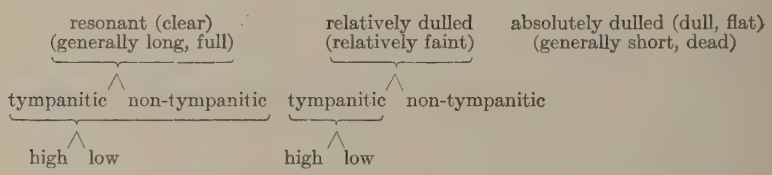
theoretic differentiation between tympanitic and non-tympanitic notes will not make the matter much clearer to a beginner; but in a practical demonstration a musical ear will very readily appreciate the distinction between the resonant but non-tympanitic lung note and the true tympanitic note of the bowels. No sharply defined boundary really exists between tympanitic and non-tympanitic notes.

Experience teaches us that a non-tympanitic note will be transformed into a tympanitic note when the tension of the air within the organ diminishes, *i. e.*, when its wall is relaxed; and the converse is also true, that with an increase in tension a tympanitic will be transformed into a non-tympanitic note. If we inflate a pig's bladder while at the same time we percuss over it, we shall notice that up to a certain point of distention the note is tympanitic, but with further inflation non-tympanitic. During the transformation of a non-tympanitic into a tympanitic note its intensity or sonority increases; in other words, the note first becomes hyperresonant before it becomes tympanitic.

The essential characteristic of a tympanitic note, as has been said, is a certain definite pitch, so that naturally we can distinguish a low tympanitic from a high tympanitic note, and gradations between the two. Different tone heights (pitch) cannot be distinguished easily in non-tympanitic notes. The pitch of a percussion-note depends upon various factors, above all, upon the tension of the wall inclosing the air-space and upon the size of the latter.

It is self-evident that more than one of the qualities discussed may characterize the same percussion-note. Thus, *e. g.*, we may speak of a relatively dulled high tympanitic note, or of a resonant low tympanitic note.

The following scheme of the tone qualities described above may be useful:



There are two other specific tone qualities which must be mentioned, viz., *metallic resonance* and the "*cracked-pot*" *sound* or *cracked-pot resonance.*

METALLIC RESONANCE[1]

Metallic resonance means a peculiar quality of the percussion-note, which is best characterized by its name. It can be imitated by percussing one's own distended cheeks with a plexor and pleximeter.

Its metallic character depends upon an individual metallic overtone of a definite pitch, which can be appreciated sometimes during the entire duration, sometimes, however, only at the end of the sound. In the latter case we speak of it as a *metallic after-resonance.*

The latter is probably due to a faint metallic resonance at first

[1] For the newer theory of the origin of metallic resonance see p. 206.

obscured by the ordinary percussion-note and audible only at the end of it.

We are especially indebted to Wintrich for the older experiments upon metallic resonance. He showed that this sound arises only when large air-spaces are percussed. These may be closed or open; but if open, the orifice must be relatively narrow, *i. e.*, in proportion to the cross-section of the cavity. The inner surface of the cavity-wall must be comparatively smooth, because, according to Wintrich, metallic resonance depends essentially upon the reflection of the air-waves which percussion sets into vibration within the cavity and their interference with one another. This produces the high, inharmonious overtones responsible for the metallic character of the sound. The thinner the walls, the easier the metallic character can be appreciated. For a criticism of Wintrich's theory see p. 206.

If the walls of the cavity be yielding (flexible), metallic resonance will not result unless they are under a certain moderate tension. Again, a cavity must be of a certain size to produce metallic resonance; according to Wintrich, its greatest diameter must be at least 6 cm. Smaller cavities very rarely furnish metallic resonance.

The metallic resonance noted in percussing the normal human body is in most cases so faint that it can be appreciated only when the ear is very near or is connected with the percussed area by means of a stethoscope (auscultatory percussion). The easiest way to appreciate metallic resonance is by means of the "stick-pleximeter" method (Heubner). In this method we percuss with the handle of the plexor upon a bit of stick, a coin, or some other firm object placed upon the body, and at the same time auscultate with the stethoscope in the immediate neighborhood. In case a coin is used, care must be taken to dull its own metallic resonance. By the reverberation of the high overtones in the "stick-pleximeter" method the resulting shrill noise seems particularly to favor the production of a metallic resonance. (See also, however, p. 208.) Metallic resonance may accompany non-tympanitic as well as tympanitic notes; but in the former case it can be appreciated only by the aid of the stick-pleximeter method of percussion.

Metallic resonance can be elicited sometimes over physiologic cavities, *e. g.*, the stomach and intestines; sometimes over pathologic collections of air, *e. g.*, lung cavities, pneumothorax, pneumopericardium.

If the cavity contain fluid as well as air, change of the patient's position may alter the pitch of the metallic resonance. This is because its pitch depends partly upon the greatest diameter of the air cavity, which would be altered by the shifting of the relative positions of the fluid and the air.

CRACKED-POT RESONANCE

(Bruit de Pot Fele; Noise of the Chink of Coins)

This peculiar clanging or rattling percussion noise can be simulated by filling the hand with coins, shutting it tight enough to allow only a slight space for the coins to move, and then shaking the hand; or, in another way, by clasping the hands together firmly, leaving a slight air-space between, and then striking the back of one hand against the knee.

The force of the blow will expel some air through the narrow chink between the hands. Another method is to strike a hollow rubber ball with a narrow opening vigorously enough to expel some air with each stroke. Such experiments, as well as the conditions in the chest which are responsible for the phenomenon, make it probable that the cracked-pot sound observed in man is a stenotic murmur following the primary tympanitic tone; the percussion blows expel air quickly through a narrow, slit-like opening. (See p. 210 for its diagnostic significance; p. 208 for the theory of its origin.)

A THEORETIC DISCUSSION OF THE PERCUSSION-NOTE, BASED UPON RECENT EXPERIMENTS

The foregoing analysis of the different qualities of the percussion-note is based partly on ordinary acoustic laws, partly on the older and rather meager experiments (of Skoda, Wintrich, Zamminer, Gerhardt, Sr., and Eichhorst), which analyzed the tones by means of a resonator, and partly on an exact comparative analysis of the tones actually heard on percussion. How important and reliable the last (subjective) method is is proved by the fact that its results have been, in almost every instance, confirmed by the recent objective experiments about to be described. We owe these experiments to A. Geigel and Theo. Selling. The latter, with Edelbaum and Scripture at F. Müller's instigation, undertook the investigation of the percussion-note by means of the newest physical apparatus.

For the comprehension of what follows it must be understood that, according to Helmholtz, there is no sharp distinction between a *noise* and a *tone*. Each can be resolved into simpler tones. Practically the boundary between them lies at the point where the ear fails to distinguish any one pitch on account of the interference of the partial tones. This distinction obviously depends to a great extent on the natural power of the individual ear. If several keys of the piano be struck together at random, the result generally gives the impression of a mere noise, on account of the difficulty of distinguishing the individual tones, although in this case the "noise" is obviously composed of musical tones, and is not very different from certain "harmonies" of modern orchestration which are tolerated by the present generation. Similarly in physical diagnosis the lack of a sharp distinction between a noise and a tone is observed in studying the transition between tympanitic and non-tympanitic percussion-notes. From both, however, the pure "tones" of Helmholtz are to be distinguished by their purely sinusoidal vibrations.

In the percussion of air-containing organs the organ and the air contained in it obviously vibrate together as a whole; so that the old discussion as to whether the resonant note of air-containing organs was produced by vibrations of the air or of the surrounding tissue was wholly futile. Vibrations of the lung substance without synchronous vibrations of the air-content are certainly as inconceivable as are vibrations of the air-content without the participation of the lung substance. R. Geigel's comparison of the percussed lung to percussed foam is, therefore, entirely pertinent.

Selling[1] first determined, by means of both Einthoven's galvanometer and the phonograph, that a resonant (lung) tone is distinguished from a dull (lung) tone by the greater amplitude of the vibrations. This corresponded exactly to the older view. He also established by both methods the more interesting fact that a resonant tone lasts longer than a dull one, thus confirming our early theory that in general a parallel exists between resonant and dull and full and dead tones. Such a parallel is, of course, not invalidated by the fact that the terms "full" and shallow express something fundamentally different from the terms "resonant" and "dull," namely, the duration of the vibration, which depends, other things being equal, upon the mass and the elasticity of the vibrating body.

Selling also investigated the pitch of the percussion-note. By means of the resonator he proved the pulmonary tone to be a very complex one, made up of many partial tones, among which the deep notes predominate. The range of pitch of the resonant, non-tympanitic pulmonary tone is from low F to high C. In healthy adults it goes down to about low A; in children to middle F; in patients with emphy-

[1] Deut. Arch. f. klin. Med., vol. xc, parts 1 and 2, p. 163. See also F. Müller, Zeit. f. ärztl. Fortbildung, 1906, parts 15 and 17.

sema to low F. The normal resonant pulmonary tone is therefore preëminently deep. The dull tone, on the contrary, is higher in pitch, since the deeper tones are subdued through the decreasing capability of the lung for vibration. All this supports the proposition (p. 203) to set aside the terms clear for resonant and muffled for dull, since one usually means by clear a high, by muffled a low, tone.

This determination of the predominance of deep notes agrees with the fact, pointed out by Selling, that the vocal (tactile) fremitus is felt only when the patient pitches his voice low. In women there is often no appreciable fremitus, since their high voices are not in harmony with the deep lung tone. In children, however, it is more perceptible than in women, since, although their voices are higher, so is also their normal pulmonary tone, on account of the smaller volume of the lungs.

According to Selling, the determination of the highest pitch of the notes composing the pulmonary tone is less important, for this depends more on the intrinsic tones of the hammer and pleximeter or of the percussing and percussed fingers. This agrees with the fact that a dull note over the lung generally seems higher, because the deep pulmonary tones are fainter, while the higher notes of the pleximeter are unchanged. Since the dull pulmonary tone is essentially a weakened tone, and since light percussion weakens the tone, it follows that in light percussion we tend to get a higher pitch, *i. e.*, one more influenced by the tones of the percussion apparatus. This is a point of some importance in the discussion of the relative merits of strong and light percussion for the determination of deep dulness (p. 215).

Selling also found the tympanitic character of a tone to be due to the greater preponderance of one fundamental tone and the partial tones near it in the scale. This has so far been determined by the resonator alone, but not through the curve of the string galvanometer.

R. Geigel's experiments chiefly refer to the determination of the conditions causing the tympanitic note and the metallic resonance, with some other phenomena of interest in physical diagnosis connected with the latter. He believes their explanation lies in the correct application of principles laid down several decades ago by Helmholtz. The differences between the ordinary resonant, the tympanitic note, and metallic resonance are, he maintains, caused by differences in conditions determining the number of overtones accompanying the fundamental. These conditions were explained by Helmholtz. He discovered that the more the vibrating body vibrates in its dependent parts, no less than as a whole, the more overtones will arise. If a stretched string be set in vibration by drawing it to one side at its middle point and releasing it, it vibrates primarily as a whole, so that the fundamental note is clearly heard. Every part of the string passes the position of equilibrium almost synchronously and in the same direction. Still, even here the movement transmitted from the initial movement of the string is not instantaneously communicated to all parts of the string, so that nodes are formed dividing the string into a certain number of equal parts, which vibrate independently in alternating directions and more rapidly than the string as a whole. These independent secondary vibrations give rise to overtones. According to Helmholtz, the number of overtones depends on the way in which the initial movement is given to the vibrating body. The more the transmission to all parts of the string is disturbed, the more overtones are formed. For instance, if instead of the string being slowly drawn to one side and released, it be struck sharply with a hammer, the movement given to it becomes more complex and the overtones are increased. The shorter the stroke, the less completely and quickly is the movement transmitted to the rest of the string: the more nodes and the more overtones are, therefore, formed. This is particularly true when the hammer is made of hard material. In that case the string gives a clanging sound. This is the reason the hammers in a pianoforte are cushioned, since the duration of contact between hammer and string is thus increased. The clanging sound of the uncushioned hammer is caused by the large number of high overtones, for in general the higher overtones are not in harmony with the fundamental tones, *i. e.*, their rates of vibration do not stand in any simple ratio to the rate of vibration of the fundamental tone. The clanging of a mass of metal when struck owes its peculiar metallic quality to such high overtones. The same causes that produce the overtones in a vibrating string produce them also in a vibrating membrane or a vibrating volume of fluid or air. Abundant overtones are caused by variations in the rapidity of vibration occurring very frequently throughout the vibrating body.

Air-containing organs, such as the lung and intestine, fall, when percussed, into permanent vibrations the same as do solid bodies and the gaseous content of hollow chambers. The percussed masses may vibrate as a whole (ground tone) or with superficial nodes (overtones). Geigel has shown what conditions determine (by

giving rise to overtones) simple, clear, tympanitic, metallic resonance. The tympanitic note is the simplest sound elicited by percussion. Here the fundamental tone and the lower overtones in harmony with it are so predominant that the ear can recognize a distinct pitch, and the vibrating mass vibrates as a whole or with only a few nodes. The non-tympanitic note contains, on the contrary, many overtones, obscuring the fundamental note. The transition from tympanitic to the non-tympanitic notes may be obtained by percussing a pig's bladder inflated with air. Up to a certain point of distention the note is tympanitic; after that, non-tympanitic (p. 204). Geigel attributes the tympanitic character of the note, in the first instance, to the fact that the comparatively relaxed and yielding wall permits a sufficiently longer duration of the contact between the wall and the percussing instrument for the movement to be transmitted to the whole bladder, so that it vibrates primarily as a whole, as does a string struck with a cushioned hammer. If, on the contrary, the bladder be markedly distended, contact is so short as to give rise to a circumscribed undulation of the surface before the movement has reached the more distant parts of the bladder. In this case, so many different portions of the bladder vibrate independently that a vast number of overtones are produced and the sound is a mere noise. Up to a certain grade, however, the ear can distinguish pitch in mere noises, so that even a non-tympanitic note may be recognized as having a deeper pitch in some cases than in others.

Geigel attributes metallic resonance to a preponderance of very high inharmonious overtones. As a rule, this naturally occurs in non-tympanitic notes. The author cannot agree with Geigel in his assumption that the existence of metallic resonance necessarily excludes the presence of a tympanitic note and vice versâ. There might be conditions where now the fundamental note, now the high overtones, predominate without detriment to the musical character of the fundamental note by a large number of lower overtones, *i. e.*, the metallic resonance need not originate in a non-tympanitic note. That a fundamental tone and metallic overtones do not absolutely exclude each other is shown in amphoric breathing, the conditions of which are the same as those of metallic resonance, and in which a deep fundamental tone as well as high overtones can be recognized. The fact that the degree of tension of the air in the percussed cavity is a determining factor in producing metallic resonance agrees with Geigel's theory, as may be shown by puncturing the chest-wall in pneumothorax. Metallic resonance occurs only over rather large air-containing cavities apparently because: (1) Small ones vibrate too easily as a whole; and (2) larger ones containing many small cavities (the lungs) possess too little elasticity to produce enough nodes. The significance of Heubner's stick-pleximeter percussion for eliciting metallic resonance lies, according to Geigel, in the fact that the blow is made exceedingly short, so that many high overtones result. The older explanation may also, however, be true (p. 205), for the high note caused by the blow on the stick reverberating from the cavity may contribute to the metallic character of the resulting sound. Geigel's explanation of metallic resonance is more satisfactory than Wintrich's, because it explains the origin of the characteristic high discordant overtones, whereas the latter's theory of reflection and interference fails to explain why the whole series of overtones which would produce the ordinary pulmonary tone does not occur.

Scant attention has been paid to the physical basis of "cracked-pot" resonance (p. 206). Though obviously related to metallic resonance, its nature and its causation are essentially different. It may possibly be due to high discordant overtones not sufficiently isolated to produce the metallic resonance. The expulsion of air through a narrow opening plays a part in causing it. Apparently the edges of the opening are set in vibration, and an opportunity is thus given for the production of high overtones by interference.

TOPOGRAPHIC PERCUSSION

PERCUSSION CHARTS; SUPERFICIAL AND DEEP DULNESS OF ORGANS; LIGHT AND STRONG PERCUSSION; SITUATION OF THE ORGANS; ORIENTATION POINTS AND LINES

Topographic percussion signifies the determination of the boundaries of the organs of the body by means of percussion. By this method we attempt to project the boundaries of the organs upon the body surface, and to represent these relations conveniently in the history sheets, the

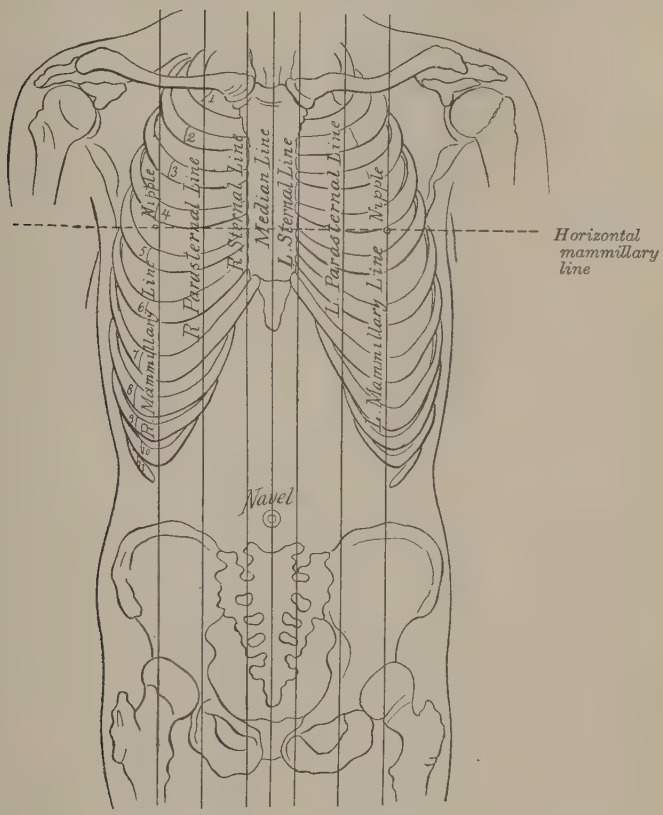


Fig. 115.—Chart of anterior body-half.

borders are sketched upon a chart of the human body, with a skeleton drawn inside. Figs. 115, 116, and 117 show such percussion charts. Perhaps they would be still more convenient if they were double the size. Since every man's skeleton is not of the same shape, it is advisable to represent by some mark, *e. g.*, a cross, the boundary points which are

quite normal in their relation to the skeleton. (See Fig. 123.) Such a chart is rarely absolutely accurate.

The possibility of employing topographic bounding of organs which partly overlap one another depends upon the fact that some are filled with air and some are solid. A solid organ gives a dull, a hollow organ a resonant, note. In rare cases the qualitative variations of the resonant note can be utilized for defining the boundaries. For example, we can differentiate the resonant but non-tympanitic note of the lung, or the low tympanitic note of the stomach, from the high tympanitic note of the intestine. But naturally the differences are often very slight, and the qualities of the resonant notes merge into one another without sharp boundaries, so that the distinction is by no means easy.

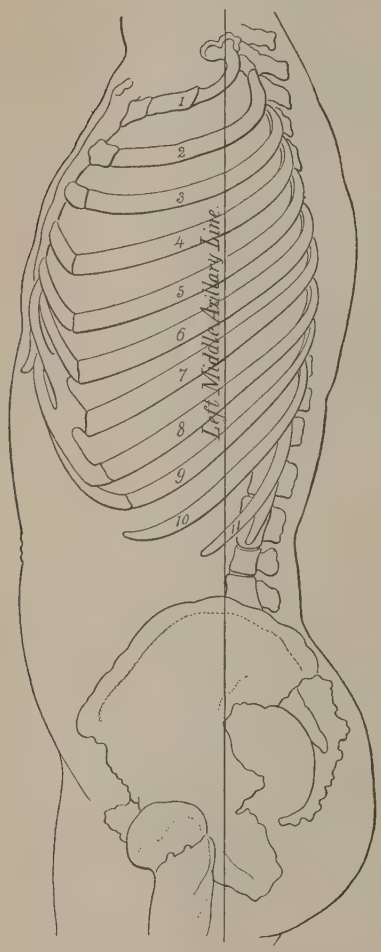


Fig. 116.—Chart of left lateral body-half.

The first essential for successful topographic percussion is to localize the percussion stroke. Where the boundaries to be defined are superficial, that is, where they lie directly under the body-wall, the lightest possible percussion will evidently succeed best. As soon as we percuss more vigorously, the blow will be transmitted too far, producing mixed tone phenomena. *To appreciate superficial boundaries, therefore, it is a good general rule that we should percuss as lightly as possible, and a good criterion of the desired strength is to evoke practically no note over the dulled areas.*[1] Then the same strength of percussion will produce a very plain resonant note just as soon as we encroach upon the edge of an organ containing air, *e. g.*, in percussing the lower lung boundary over the liver.

Special attention should be directed to another point in determining the superficial boundaries. The skilled observer instinctively heeds it; but the beginner, despite his best endeavor to percuss lightly, disregards

[1] This is the method of percussion which Goldscheider has recently named "*threshold percussion*," but curiously enough he recommends it for percussing the deep cardiac dulness and not for superficial dulness. (See p. 216.)

it, and so fails in a correct differentiation. *It is not only necessary to percuss lightly, but the pleximeter or the finger of the left hand serving this purpose should be brought into very light but perfect contact with the surface of the body.* The mere weight of the finger is sufficient. Firm pressure of the pleximeter (or finger) will simulate the effect of strong percussion, because the impact of the percussion will penetrate much more intensely, further into the depths and to the sides, and so prevent a linear localiza-

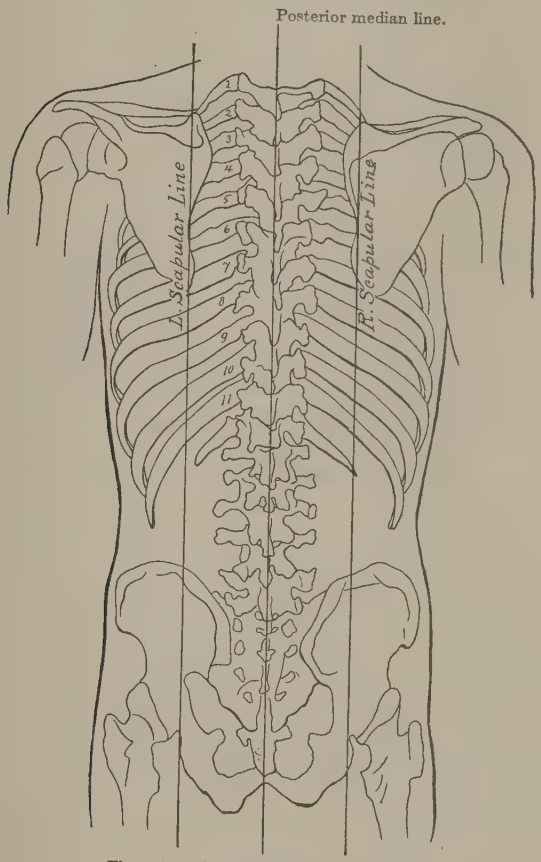


Fig. 117.—Chart of posterior body-half.

tion of the boundary between two superficial organs, the one containing air and the other solid.

The whole secret of success in percussing superficial boundaries depends on these two principles—light percussion and light contact.

The rationale of such light contact between pleximeter and body surface is founded upon the following considerations: Discontinuity of the thoracic vibrations, essential to localize the percussion impact properly, can only be secured in this

way. The light application of the pleximeter materially shortens in duration the influence of the percussion stroke in that the percussion impact is transmitted to the thorax for the shortest possible time, namely, during the moment when the percussion blow itself causes a more intimate contact between the pleximeter or pleximeter finger and the chest-wall. There is no such transmission before this brief moment, because the contact is not sufficiently intimate, nor after it, because the rebound of the pleximeter again interrupts the contact. This abbreviation, interrupting the impact action, prevents any considerable transmission of the mechanical impression along the body surface, and therefore secures a sharper lateral localization. It further eliminates a considerable part of the percussion power and so accomplishes the weakest possible percussion.

Disregard of this essential factor, light contact, robs supposedly light percussion of the greater part of its advantages and explains the poor percussion results obtained by many observers who lack confidence in this method. On the other hand, the author has noticed that even beginners learn to percuss superficial boundaries correctly in a very short time, ever since he has laid great stress on this point in his teaching. Even for comparative percussion (see p. 258) this method has decided advantages in the determination of very slight superficial dulness, *e. g.*, small consolidations of the lung.

This light percussion for estimating superficial boundaries is called briefly *superficial percussion;* and the dulness mapped out by the method is called *superficial dulness*. It is the easiest for the beginner to differentiate. Its position and extent generally correspond quite accurately to the position of the part of the organ adjacent to the body-wall.

So much for the determination of superficial boundaries; in many cases, however, the boundaries of organs which we wish to differentiate lie in the deeper parts, *e. g.*, most of the heart is covered by the lungs, and yet it is very desirable to estimate its size by percussion. Naturally this is a much more difficult differentiation than that of superficial boundaries. The blow must, of course, penetrate the tissues to the depths of the organ in question, in order to obtain tone differences sufficient to determine, at least approximately, the position of the deep-lying boundaries. The intensity of the note will depend upon the thickness of the layer of air that we percuss. The more air-containing tissue that is set in vibration, the louder (more resonant) the note. If *a b* (Fig. 118) represent a cross-section through the anterior wall of the thorax, and *c d* one through the heart, then by moderately strong percussion in the direction of the arrows *e* and *f* the shaded elliptic areas will be set in vibration.[1] Weil has named such an area "the acoustic sphere of action of the percussion blow."

For reasons which follow later the author considers this expression unfortunate and prefers to substitute for it "sphere of the blow" or "area of the blow." The elastic vibration transmitted into the deep tissues within the area of the percussion blow is responsible for the acoustic phenomena in percussion. At a certain depth, the inner boundary of the blow, the resistance of the tissues reduces these vibrations to zero. Then an elastic recoil reflects the vibrations to the body surface and so produces the sound. The phenomenon resembles striking a violin string, with the difference that the percussion blow vibrates the tissue in three dimensions of space, whereas the violin string vibrates but in two. The elasticity of the parts produces not only to-and-fro vibrations, but also contributes periodic secondary elastic vibrations, just as with the violin string, and thus conditions essential to the production of tone phenomena result. According to this conception, the movement impulse

[1] It is probably unnecessary to explain that the shapes of these areas, represented in the figure as perfectly regular ellipsoids, are purely hypothetic, for naturally the percussion stroke is not transmitted the same distance into the solid heart as into the lungs which contain air and are elastic. The former is dislocated by the stroke practically in toto, whereas the lungs are elastically compressed. The general proposition, however, is in no way altered by this peculiarity.

for the percussion-note proceeds from the primary deformity of the tissues within the sphere of action of the blow; and the strength of this impulse is estimated by the formula: the energy, $E = \frac{\text{mass} \times (\text{velocity})^2}{2}$. Hence, it is evident without further discussion that the intensity of the resulting note which depends upon this energy within the sphere of the blow, other things being equal, is proportional to the mass or volume, mainly the depth of tissue affected by the blow. Practically, this is limited to the air-containing tissue, because the solid organs destroy the note. Hence, in percussing over an air-containing organ toward the border of an adjoining solid organ the intensity of the note will diminish as soon as the sphere of the percussion blow reaches to the solid organ.

Percussion at *e* (Fig. 118) will elicit a resonant note, whereas at *f* (when the sphere of the blow reaches the heart) a so-called "relative" though not an "absolute" dulness will be appreciated. The nearer the blow approaches the solid organ, the duller the note, until at the point where the solid organ reaches the surface the note becomes absolutely dull or flat—*superficial dulness*. More deeply situated organs can under some circumstances be outlined by the position of a relative dulness. The percussion adjusted to bring out this type of dulness is called *deep percussion* and the resulting dulness *deep dulness*. The pleximeter or the pleximeter finger must be applied lightly to determine even deep dulness, but so that the contact with the body surface is perfect.

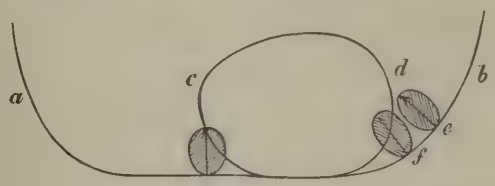


Fig. 118.—The acoustic spheres of the blow in deep percussion—origin of the deep dulness.

The effect of this precaution, which, by the way, is not generally appreciated, has already been discussed (p. 211). The latter vibrations of the percussion stroke in comparison with those directed deeply are diminished and the area of the blow forms a narrower ellipse and so naturally defines the boundaries of deep organs more exactly.

In addition to applying the pleximeter lightly the examiner must avoid too strong a percussion blow, so as to prevent lateral transmission as much as possible, because strong percussion prevents any exact localization.

For superficial percussion the percussion stroke should be as light as feasible, so as to include as small a sphere of the blow as possible; but for deep percussion the strength of the stroke and the contact of the pleximeter should be adjusted so that the sphere of the blow will just include the deep-lying organs (as is shown in Fig. 118). To accomplish such a result deep percussion need in reality be only a little stronger than superficial percussion. The not uncommon designation of deep percussion as "strong percussion" is unfortunate. The finer results even of deep percussion cannot be demonstrated to a circle of listeners at any distance from the examiner. Percussion strong enough to accomplish the latter purpose produces, for the most part, incorrect results and is at best only available for the demonstration of gross relations.

The exact strength of percussion and the approximate firmness of contact of the pleximeter are very difficult for a beginner to learn and require long practice. A helpful plan is so to adjust the strength of percussion and the degree of contact of the pleximeter as to *produce the most intense dulness and to bring out the differences between the notes as plainly as possible.*

The above conception, viz.: that the deep dulness of organs depends only upon the volume of the air-containing parts in the region of the sphere of the blow were first advanced by Weil, and according to the author's belief represents not only decided progress in our theoretic knowledge, but also a firm basis for the rules of percussion given above and practised successfully for years.

It was formerly believed that the solid organs themselves not only produced a slight tone, but were even capable of partially dulling the loud resonant tone of the neighboring air-containing organs. According to this hypothesis the deep dulness depended upon the dulling influence of the solid organs in the neighborhood of those filled with air. Weil [1] has experimentally proved that such dulling influence does not exist.

An attempt has been made to discredit this conception of deep percussion, and although based upon physically incorrect premises, the arguments, nevertheless, merit a brief mention. It has been claimed that the vibration produced by even the lightest percussion penetrates deeply into the body, so that the above-assumed sphere of action of the percussion blow is incorrect. This claim was based largely upon the following experiments: Light percussion upon the anterior surface of the thorax sets into vibration a sensitive flame attached to its posterior surface; further, with light percussion a great difference in the resulting note depends upon whether the individual examined lies upon a hard support, upon a mattress, or upon an air-cushion; and finally percussing a man standing against a door decidedly alters the note. Arguments opposing the theory of the limited sphere of action of the blow which are in part founded on these long-recognized facts are, so it seems to the author, based upon premises which are inaccurate from the standpoint of physics. The experiments prove merely that even when percussion is light, *sound vibrations* may penetrate the entire body and may cause phenomena of resonation on the opposite side to that percussed, *i. e.*, they may be influenced by resonance, and so influence the result. This is quite as comprehensible as the conduction of the percussion-note to the examiner's ear. However, perhaps a part of each experiment shows that in percussing upon the anterior surface of the bony thorax the stroke is conducted through the skeleton and around the lungs to the back. But none of the experiments show anything about the behavior of the *primary action of the percussion stroke* in *the interior of the air-containing organs,* although this must essentially influence the percussion-note. These critics have not carefully analyzed the process of percussing deep-lying organs. The author's presentation emphasizes the importance of defining the *primary* sphere of the percussion blow over air-containing organs as that part of these organs, generally ellipsoidal, into which the mechanical action of the blow penetrates before it is destroyed by friction. The relatively light percussion recommended by the author does not penetrate very far on account of the softness of the affected organs, which absorbs the shock of the impact as soft earth lessens the mechanical effect of a bullet or a cushion the impact of a billiard ball. This direct or primary action of the percussion blow itself must not be confused with the tone vibrations. The latter, as already emphasized, are more the consequences of the primary impact, depend upon the elastic recoil of the tissues

[1] A. Weil, Handbuch und Atlas der topographischen Percussion, Leipsic, 1877. Pleural effusions only apparently produce a dulling influence, the Rauchfuss or Grocco triangle, upon the healthy side of the thorax. (See p. 265 et seq.) For unless the examiner is very careful to minimize the strength of his percussion stroke upon the healthy side, some part of the exudation adjacent to the vertebral column will necessarily be included in the sphere of the blow. When even the lightest possible percussion elicits such a triangle of dulness, it is because the effusion of the affected side crowds the lung upon the healthy side and diminishes its air-content.

directly affected by the primary stroke; and can, therefore, naturally be transmitted through the entire body of the person examined to its posterior surface and even through the air of the room to the observer's ear, since, as a result of the slight excursions of the parts vibrated incident to their production, tone vibrations penetrate almost all bodies readily and to a great distance. This, however, is quite a different type of movement from the primary action of the blow. The conditions may perhaps be made clearer to the reader by comparing the primary action of the blow in the region of the so-called sphere of action of the percussion stroke to the primary excursions of a tense violin string struck by a hammer. As soon as the hammer rebounds, the string vibrates to and fro, producing the tone vibrations of the surrounding air and of the sounding board. Or we can directly compare the sphere of the percussion blow, the originator of the tone, to the violin string pushed from its position of unstable equilibrium, and the remainder of the body, together with its surroundings, to the sounding board which shares in the vibrations. Other things being equal if the resonator of the violin remain constant, the intensity of a tone arising from the blow upon the string depends upon the energy of the vibrating string. In the same way the intensity of the percussion note in deep percussion is proportional to the energy of the sphere of the blow. Now, since, as we saw above, this energy can be estimated according to the formula $E = \frac{\text{mass} \times (\text{velocity})^2}{2}$, so, other things being equal, the size of the sphere of the blow, so far as it involves tissues capable of vibrating, *i. e.*, air-containing tissues, is all important for adjusting the strength of the percussion blow. Hence, the author considers that it is possible, as has been done now for years, to outline by means of percussion the boundaries of the deep-lying organs, especially the heart; and that Weil is correct in his contention that another explanation, which could only consist in assuming a tone dulling influence of the solid organs, can be excluded on experimental grounds. No other explanation is logically conceivable. The fault with the authors who undertook to dispute this well-founded view seems to consist in their being unable to differentiate the simple action of the stroke of percussion, *i. e.*, the primary cause of the tone, from the tone vibrations themselves, *i. e.*, the secondary cause of the tone. Weil's teaching took an exception to this attack, but the above analysis of the physical relations is given by the author for the first time here. For the sake of clearness and simplicity it is advisable to accept the author's substitutes "sphere of the percussion blow" or "sphere of action of the percussion blow" instead of Weil's term, "acoustic sphere of action of the percussion blow," because the sphere of action is here essentially mechanical and not at all acoustic.

The necessary strength of the percussion stroke naturally depends not only upon the nature and the position of the surrounding organs, but upon the thickness of the body-wall, and especially upon the dimensions of the body. For example, the inferior lung boundary can ordinarily be easily distinguished from the liver by very light percussion, but not in very fat or edematous patients, because then the sphere of action of the percussion blow does not penetrate beyond the thick layer of the thoracic wall. In such cases only very vigorous percussion can bring out a clear, distinct pulmonary resonance, and at best the superficial as well as the deeper boundaries are very difficult and sometimes impossible to map out. It goes without saying that in percussing children the strength of the percussion blow should be modified to correspond to their smaller size.

It is evident that the strength of percussion adjusted to bring out the deep dulness is by no means always the same. Fig. 119 (see next page) will perhaps best illustrate this point:

It represents a horizontal cross-section through the thorax with the heart surrounded by the lungs. The areas of two different percussion blows are represented in the figure, one penetrating deeply (stronger percussion) and the other more superficial (lighter percussion); yet both outline the border of deep cardiac dulness at the same point, *x*, because, according to Fechner's psychophysical law, the shaded portion of the heart substance *ab* furnishes as plain a diminution of the tone to lighter percussion as the much larger portion *cd* does to stronger percussion. This essenti-

ally coincides with practical experience and best explains the remarkable dispute which has recently been so warmly undertaken over the elementary questions of percussion strengths and the percussion of the deep cardiac dulness. The author believes that there is right upon both sides, and that deep dulness can be correctly brought out by different strengths of percussion provided that the examiner has properly learned how to percuss. The quality of the examiner's ear is a very essential factor. This is evident when we remember (see p. 207) that the pitch of the percussion-note must be assumed to vary with the strength of percussion. This influence of the strength of percussion upon the pitch is one reason for the individuality of percussing for deep dulness, because each observer, depending upon the quality of his hearing, must percuss in such a fashion as to bring out varieties in notes most plainly for himself. Detailed rules for the strength of percussion are superfluous. It is fortunate that such liberty in percussion does exist, otherwise no results could have been obtained with deep percussion; and one might think, by reading many of the latest publications upon cardiac percussion, that nothing had been accomplished. Percussion must remain a free art, and the only valuable rule (p. 214) is *that the strength of percussion as well as the force with which the pleximeter is applied must be so regulated that the examiner's ear appreciates the maximum degree of the dulness and the most distinct dulness.* This may vary with the patient and with the examiner, or rather with the latter's ear, from all grades of medium strength to very light percussion, but it should never be exceptionally strong.

Goldscheider[1] has practised a so-called "schwellenwert percussion" (threshold) to determine deep cardiac dulness. He employs the lightest possible percussion, and it is actually so faint that one is unable to appreciate any distinct note over the deep cardiac dulness, whereas on the other side of the borders the note is just audible.

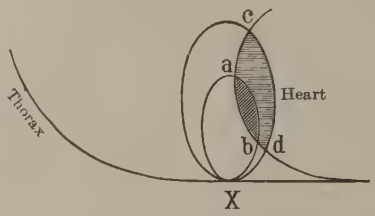


Fig. 119.—Diagram to show that different strengths of percussion may outline the same deep heart dulness.

He, therefore, employs for the deep dulness the rules which the author has suggested for the superficial dulness. (See p. 210.) The deep dulness may doubtless be outlined with even as light a percussion as the author ordinarily employs for mapping out the superficial dulness, and, in fact, the author has several times convinced himself of this possibility.[2] But, on the other hand, there are many cases in which this method will not accomplish any result, or at best too restricted a deep dulness or one lying too near the superficial dulness. This depends upon the peculiarity of the cases themselves; and Goldscheider acknowledges further that his lightest percussion does not always succeed. The author does not recommend Goldscheider's method, because it does not depend upon any generally applicable acoustic principles, and because it disregards the didactically important distinction between deep and superficial dulness. He does, however, appreciate its value in teaching others the disadvantage and lack of necessity of employing so strong a percussion as to be disagreeable to the patient. Goldscheider's excellent results may depend upon other peculiarities in his methods. He percusses upon the bent first interphalangeal joint of the second finger or upon a pencil-like stick obliquely applied at one end. Further he utilizes the intercostal spaces exclusively. With this method, in virtue of the small surfaces of contact of the pleximeter with the body surfaces, a comparatively elongated narrow region of the percussion blow is formed, favorable to the differentiations of the dulness. Goldscheider's method of sending rays of sound from the end of a little

[1] Deut. med. Woch., 1905, Ueber Herzpercussion, Cong. f. inn. Med., 1907; Deut. med. Woch., 1907, No. 28, p. 1122.

[2] In mapping out the superficial dulness one must actually percuss again, rather harder inside the deep cardiac dulness, in order to again obtain the pulmonary note, although this seems paradoxic.

stick, and, according to its position, in varying directions into the interior of the body, seems, from the physical standpoint, untenable (see p. 202), for with percussion there are no sound rays. The author's objections to sagittal percussion always perpendicular to the body surface, which Goldscheider especially recommends, and which is responsible for the term "orthopercussion," have already been expressed. (See p. 201 et seq.)

The conformity of deep percussion with the anatomic projection of the deep organs or with the results of orthodiagraphy is discussed under the comparative relations of the cardiac dulness. (See p. 201.)

If we only percuss lightly enough and with slight pleximeter pressure, *superficial dulness* is frequently quite intense. For this reason it is often called *absolute dulness*. On the other hand, deep dulness is never complete or absolute, and hence is called *relative dulness*.

The designations *absolute* and *relative dulness* should be avoided in topographic percussion, because in mapping out organs it is much more important to know whether a dulness is obtained by deep or by superficial percussion than whether it is more or less intense. Despite light percussion, superficial dulness will not be absolute if the air-containing surroundings be set in vibration.

It is easier to teach practically the other essentials to the technic of topographic percussion than to describe them. In mapping out an organ the beginner should compare the note in two places, one of which plainly lies outside and the other inside the edge of the organ to be defined. He should then percuss between these two places, gradually advancing the pleximeter parallel to the edge to be determined until one point of the boundary is determined and marked upon the skin with a pencil. In a similar way other points of the boundary are marked, and finally all are joined by a line which will correspond pretty accurately to the edge of the organ. Such a line can be represented schematically (as described above) upon a chart.

It is important to represent the points determined as round dots, because in determining the remaining points one is too easily influenced by autosuggestion from previously drawn lines.

For rapid and comprehensive registering of the results of percussion we use in the Bern clinic different colored pencils. We represent the superficial dulness obtained by light percussion by blue; the deep dulness obtained by strong percussion by red. The intensity of the dulness is expressed by varying the intensity of the color. A dulness appreciable both to deep and superficial percussion is represented by a mixed red and blue color. Even color tones and evenly mixed colors are easily made by using very soft pastel pencils and a leather stump. In order to distinguish the boundaries of organs which are palpable from those which we obtain by percussion, the former are denoted by a continuous black line. This method of representation is followed throughout this book.

A comprehension of the topographic results of percussion naturally presupposes an exact knowledge of normal visceral topography. Many anatomic facts relative to the position of organs do not, of course, apply accurately to such relations in the living body, because the position of the organs is markedly influenced by the breathing, and because even the median vital position of the thorax and of the diaphragm is quite different from that in the cadaver. This is especially noticeable in the position of the lung edges. In the first place the lung boundaries in the

cadaver assume an entirely peculiar position of equilibrium, on account of the elastic relations of the thorax and of the lungs, the rigidity of the respiratory muscles, etc. This is, or at least may be, essentially different from the median position in the living. The cadaveric position of the lung edges is generally that of exaggerated expiration. Frozen sections, inserting needles through the lung edges before opening the thorax, or

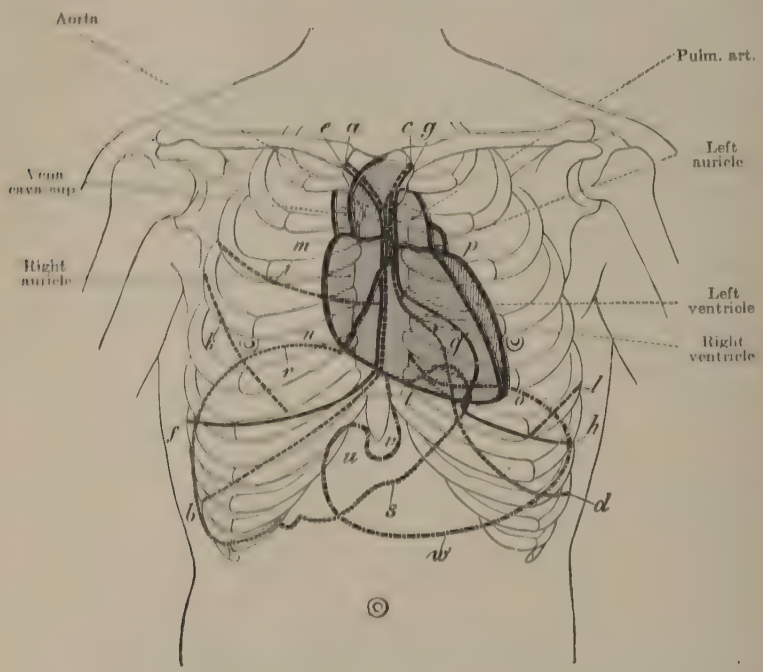


Fig. 120.—Position of the thoracic and upper abdominal viscera from in front: *a b*, Boundary of right pleural cavity; *c d*, boundary of left pleural cavity; *e f*, edge of right lung; *g h*, edge of left lung; *i*, upper incisura lobularis (right lung); *k*, lower incisura lobularis (right lung); *l*, left incisura lobularis; *m n*, right, *n o* lower, *p o*, left border of heart; *q*, mediastinal sinus situated between the pleural boundaries and the incisura cardiaca of the anterior edge of the left lung; *r*, highest point of the liver, overlapped by lung; *s*, lower edge of liver; *t*, pars cardiaca; *u*, pars pylorica; *v*, lesser curvature; *w*, greater curvature, of the stomach (modified from Luschka-Weil).

cutting windows in the thoracic wall without disturbing the costal pleura, furnish correct results. All other anatomic testimony is, in the nature of things, worthless, because as soon as the thorax is opened, the lungs are retracted, tending to assume a position of equilibrium. Topographic percussion is therefore a valuable aid to anatomists for determining the anatomic position of organ boundaries during life. The cuts illustrating the position of the viscera in this book are taken from the classic

plates of Luschka and the models of Ferber.[1] They have been drawn especially for clinical purposes to show the median position of the movable organs, and with particular attention to the sources of error mentioned above. The reader is recommended to study Ferber's models.

Symington's[2] cross-sections [or Dwight's Frozen Sections of a Child. —Ed.] illustrate the topographic relations in the child.

Figs. 120–122 reproduce outlines from Luschka's plates. To orient one's self in regard to the positions of the borders to the skeletal points, the

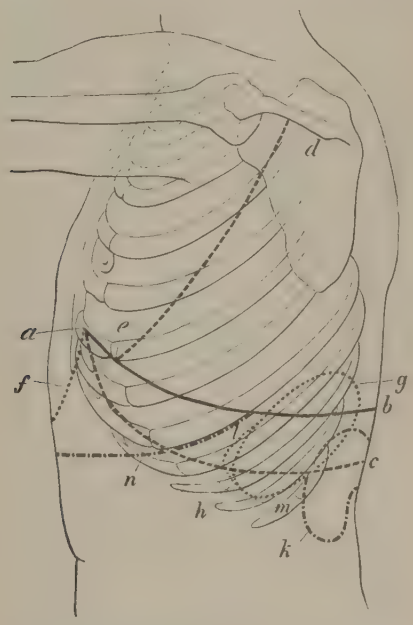


Fig. 121.—Position of the thoracic and upper abdominal viscera from the left side: *a b*, Lower edge of the left lung; *a c*, lower boundary of the pleural cavity; *d e*, incisura interlobularis; *f*, edge of the left lobe of the liver; *g*, posterior, *h*, anterior end of the spleen in its oval form; in the rhomboid form the piece (*l h*) pushes itself in between the anterior (*g l*) and the posterior (*g h*) edge; *k*, convex edge of the left kidney; *l*, splenic lung angle; *m*, splenic kidney angle; *n*, the part of the greater curvature of a moderately distended stomach lying against the wall (from Luschka-Weil).

ribs and the vertebral spines are counted. Here it is well to remember: The second rib is usually marked upon the sternum by the angle of Ludwig; it is ordinarily the highest rib which we can plainly grasp between the fingers from in front. Generally, the first rib is almost hidden beneath the clavicle. The lowest of the ribs which are directly attached to the sternum (true ribs) is the seventh. The first of the "floating ribs," *i. e.*,

[1] Situsphantom der Organe der Brust und oberen Bauchgegend, Bonn, Max Cohen & Son, 1877.

[2] Topographic Anatomy of the Child, Edinburgh, 1887.

those with their tips freely suspended, is the eleventh. In counting the vertebral spines we generally begin with the seventh cervical. Its prominence when the head is bent forward (vertebra prominens) makes it easy to recognize. Where three vertebral spines are quite prominent in this region, the seventh is usually in the middle. Where the seventh cannot be positively determined, the vertebræ should be counted from below, *i. e.*, from the fifth lumbar vertebra upward. The lower angle of the scapula, with the arms hanging, ordinarily corresponds to

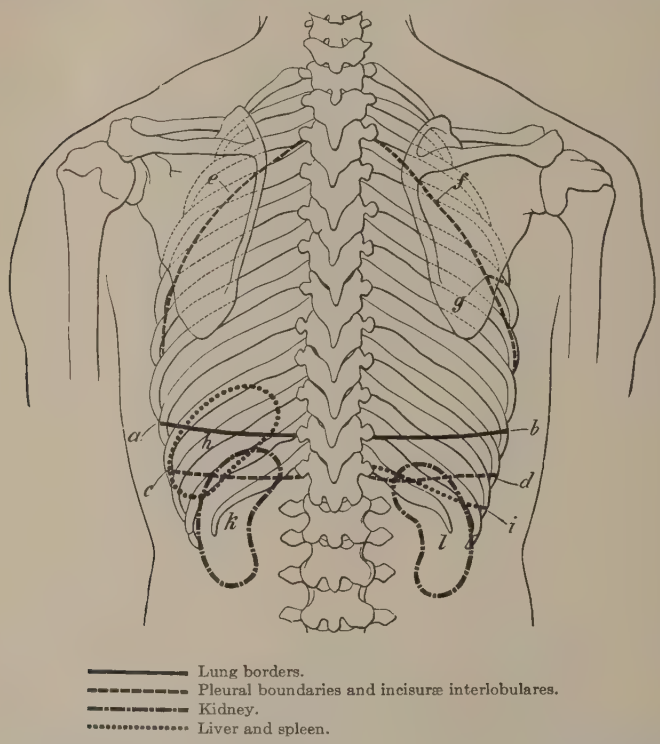


Fig. 122.—Position of the viscera from behind: *a b*, Lower lung border; *c d*, lower pleural boundary; *e* and *f*, incisuræ interlobulares; at (*g*) on the right side it is divided into the sulcus interlobularis dextra superior and inferior; *h*, spleen; *i*, lower liver edge; *k*, left kidney; *l*, right kidney (from Luschka-Weil).

the seventh rib and the seventh dorsal vertebra. The base of the xiphoid cartilage can be utilized in topography, but its tip varies considerably in length and position, and is therefore unreliable.

Besides the skeletal parts we make use of so-called orientation lines. These are vertical lines which intersect the ribs at certain angles. They are the following (see Figs. 115, 116, and 117):

1. The anterior and the posterior median line.

2. The right and the left sternal line—drawn vertically through the edges of the sternum.

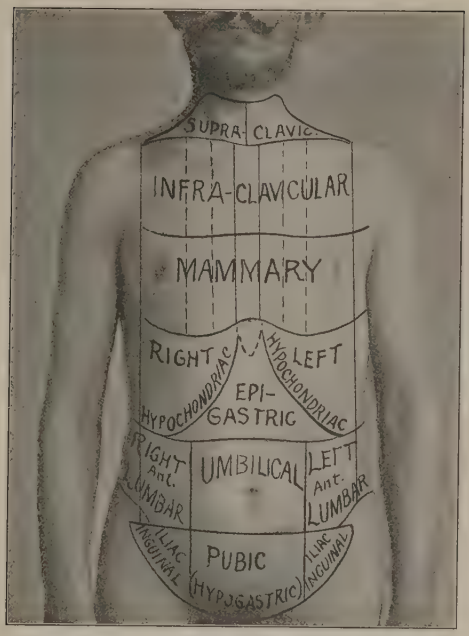


Fig. 123.—Topographic areas of trunk (anterior view).

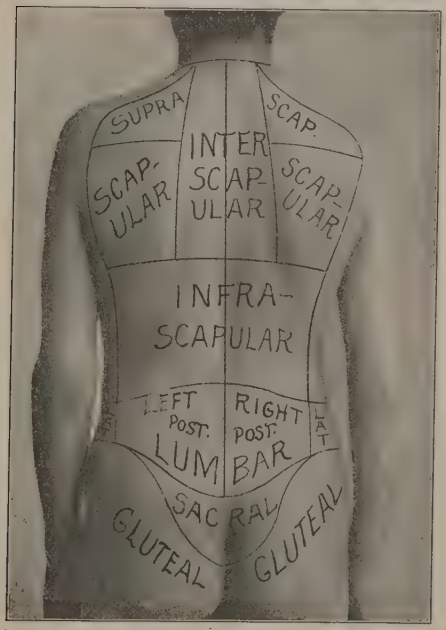


Fig. 124.—Topographic areas of trunk (posterior view).

3. The right and the left parasternal line—drawn half-way between the sternal border and the nipple.

4. The right and the left mammillary line (or nipple line)—drawn perpendicularly through the nipple.

5. The middle, the anterior, and the posterior axillary line—drawn through the apex and the anterior and the posterior edge of the axilla.

6. The right and the left scapular line—drawn perpendicularly through the inferior angle of each scapula, with the arm hanging down.

The position of the mammillary line is inconstant both in men and in women. The so-called *midclavicular line,* which is dropped perpendicularly from the middle of the clavicle, is therefore a more accurate landmark. A horizontal mammillary line is sometimes employed; that is, a horizontal line on the surface of the thorax, drawn through the nipples. Its position is, of course, influenced by the height of the latter. In men these are usually found to be between the fourth and fifth or upon one of these ribs (rarely between the fifth and the sixth ribs), about 10 cm. distant from the lower thoracic edge, and about 16 cm. from the lower edge of the clavicle.

The terms used in topographic anatomy are usually serviceable in topographic percussion—such as supraclavicular and infraclavicular fossæ, supraspinous and infraspinous fossæ, interscapular space, epigastrium, hypochondrium, mesogastrium, hypogastrium, etc. (See Figs. 123 and 124.)

TOPOGRAPHIC PERCUSSION OF THE LUNGS

THE POSITION OF THE DIAPHRAGM AS DETERMINED BY ORTHODIAGRAPHIC EXAMINATIONS

The situation of the lung borders depends upon the position of the diaphragm, which in turn is essentially connected with the position of the dome of the diaphragm. Yet the dome's pronounced convexity precludes any close parallelism between it and the lung borders. Hence, the results of orthodiagraphic examinations of the diaphragm (see p. 227) may well be presented here as anatomic studies upon the living in order to round out our anatomic knowledge of the topographic percussion of the lungs.

By means of orthodiagrams Dietlen[1] determined the highest point of the diaphragm upon each side and tabulated his results as follows:

Average Position of the Diaphragm. Estimated in Per Cent. of the Number of Cases Examined.—(*Dietlen.*)

No. Cases.			Third Rib.	Third Intercostal Space	Fourth Rib	Fourth Intercostal Space	Fifth Rib	Fifth Intercostal Space
106	Right	Males . .	. . . . .	. . . . .	25	37	38	0
70		Females	4	17	49	16	14	0
106	Left	Males . .	. . . . .	. . . . .	10	28	60	2
70		Females	. . . . .	3	38	28	31	0

It is evident from these figures that the diaphragm has, on the average, a higher position in women than in men (see Fig. 135, p. 232); that the size of the body has no influence, and that the shape of the thorax is of more significance; thus, the long narrow trunk corresponded more frequently to a low-placed and the short, broad thorax to a high-placed diaphragm. Dietlen, however, did not find this latter relationship nearly so constant as he did the connection between the height of the dia-

[1] Deut. Arch. f. klin. Med., 1906, vol. lxxxviii.

phragm and the age; thus, with increasing age the diaphragm is placed lower. This entirely agrees with anatomic and percussion studies. The highest positions of the diaphragm (third rib and third intercostal space) occurred only in females and in the four earliest decades. From orthodiagraphic studies upon the relative dislocation of the heart (see Fig. 132, p. 231) it is evident that the dome of the diaphragm is, as a rule, depressed in the erect position.

NORMAL LUNG BORDERS

The boundaries of the lungs normally move with respiration; hence we must distinguish, on the one hand, an *expiratory* and, on the other, an *inspiratory* position. This distinction is especially important for determining the mobility of the lung edges. In general, the mean position of the lung borders when the patient breathes superficially is sufficient for most purposes. The excursion of the lungs is then hardly greater than the limits of error which are inherent in percussion. The boundaries designated as normal correspond to such a mean position of the lung edges.

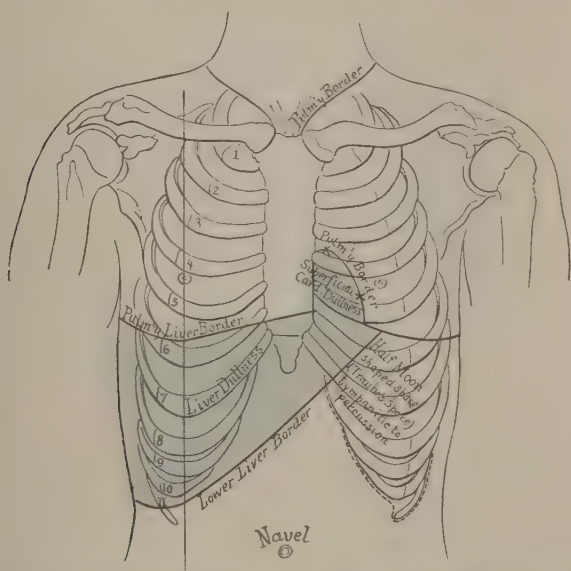


Fig. 125.—Normal percussion boundaries of the lungs, liver, and spleen, and Traube's space (anterior view).

We usually determine the inferior boundaries of the patient's right lung (the lung-liver boundary) anteriorly while he is lying down; posteriorly, while he is sitting or standing. Such a boundary line intersects the parasternal and midclavicular lines at the upper edge of the sixth rib; the axillary lines, at the eighth to ninth ribs; the scapular line, at the tenth rib; the posterior median line, at the eleventh vertebral spine. The border, therefore, is very nearly horizontal. (See Figs. 125, 126, and 128.)

The precordial edge of the left lung forms a notch within which the heart lies directly against the thoracic wall. This notch corre-

sponds to the so-called *superficial cardiac dulness* (Figs. 125 and 126). The border of the lung bounding this area lies above at the left edge of the sternum, upon the fourth rib, and runs from there horizontally to the left; at the parasternal line it curves downward to the level of the sixth rib, and then takes the same course as the inferior border of the right lung. For practical purposes we may assume that the inferior lung edge, with the exception of this notch about the heart, follows practically a horizontal and symmetric course upon both sides. The edge of the left lung which forms this notch can be easily and accurately differen-

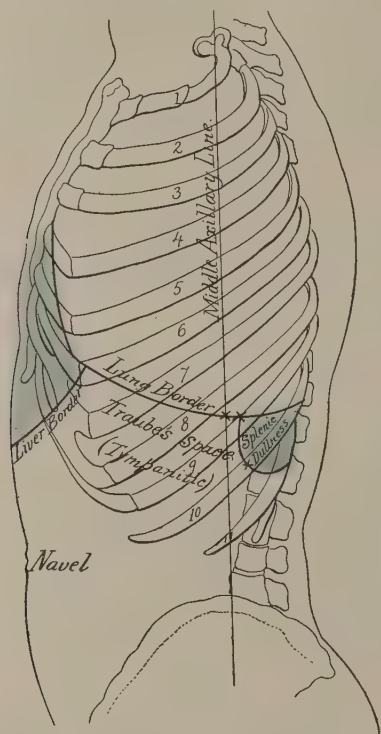


Fig. 126.—Percussion boundaries of the lung, liver, and spleen, and Traube's space (from the left side).

tiated from the superficial cardiac dulness; but farther to the left the loud, resonant note of stomach is apt to confuse the percussion. From the axillary line backward it is easier to define the edge of the lung because the spleen, the powerful muscular masses of the quadratus lumborum, and the lumbar portion of the diaphragm lie below the lung.

The anterior lung borders run almost vertically beneath the sternum (Fig. 120), and are not accessible to percussion because only a small space exists between them, and because an exact localization of the percussion stroke upon the sternum is very difficult. The bone vibrates to percussion more or less as a whole, like a great pleximeter, and transmits

the vibration widely over the surface. The superficial cardiac dulness can be percussed accurately only when a considerable part of that bone overlies or is bounded by dull-sounding tissue. (See Figs. 139, 142.) For this reason the right border of the superficial cardiac dulness ordinarily corresponds to the left edge of the sternum, and hence has usually little diagnostic importance.

The apices of the lungs above the clavicles form comparatively voluminous cones covered by relatively thick layers of muscle, which render the upper pulmonary boundaries much more difficult to determine as linear projections than the lower. Moreover, the trachea lies in such close proximity to the lung apices that percussion is very likely to set it in vibration. Hence the difficulty of properly percussing the apices. Figs. 125 and 128 represent the boundary lines of the lung apices in individuals who are neither too muscular nor too fat. The highest point of the upper lung border lies from 3 to 5 cm. above the clavicle.

The lung borders vary somewhat according to the age of the patient. For example, in old people the lung-liver boundary is situated somewhat lower (about one intercostal space). The superficial cardiac dulness is often somewhat diminished and situated about one intercostal space lower than in young adults. This change depends upon the diminished elasticity of the senile lung. Many clinicians denote this change as senile emphysema, provided nothing else abnormal is detected. The author doubts if such nomenclature be correct. He has been unable to determine a higher level of the pulmonary borders in children than in perfectly healthy adults.[1]

ACTIVE AND PASSIVE MOBILITY OF THE LUNG BORDERS UNDER NORMAL AND UNDER PATHOLOGIC CONDITIONS

Vigorous respiration will depress the lung borders several centimeters during inspiration and elevate them the same distance during expiration (*active mobility*). Percussion will very plainly demonstrate this. In the axillary line the extreme positions of the lung border may reach 4 cm. above and below the mean, so that the total excursion may be as much as 8 cm. Litten's diaphragm phenomenon (p. 85 et seq.) is the visible expression of such excursions. Deep inspiration may almost or entirely obliterate the superficial cardiac dulness.

Change in a patient's position will demonstrate a *passive mobility* of the lungs. Changing from the dorsal decubitus to the erect posture may elevate the lung-liver boundary—or very rarely depress it. In some cases no change is noted. This variable result probably depends upon the preponderance of one of two opposing factors which influence the position of the diaphragm: (1) the weight of the liver; and (2) the increased abdominal pressure due to the contraction of the abdominal muscles in the upright posture. If the abdominal walls be muscular enough to contract vigorously in sitting and standing, a slightly higher position of the inferior lung boundary seems to be the rule, because the intra-abdominal pressure will be increased. This is especially applicable to the sitting posture, whereas if the abdominal walls be relaxed, *e. g.*, the characteristic pendulous abdomen, the opposite effect will be observed, because the weight of the liver will depress the diaphragm. Diagraphic examinations have not invalidated these findings. They have shown regularly a descent of the heart and a flattening of the diaphragmatic arch when the erect posture is assumed. But this result

[1] Sahli, Die topographische Percussion im Kindesalter, Bern, Dalpsche (now Franckesche) Buchhandlung, 1881.

will not mean a change in these lung boundaries. One would think that while the dome of the diaphragm itself is depressed, the liver is raised by leverage on a frontal axis, elevating the diaphragm and border of the lung. Changing from the dorsal decubitus to a lateral posture will depress the pulmonary border of the uppermost lung about 3 or 4 cm. at the axillary lines. A deep inspiration while this position is retained may bring the border about 9 cm. lower than in the dorsal decubitus with median respiratory position; and with a full expiration in the latter posture the lung border may, under some circumstances, make an excursion of as much as 13 cm. By means of all these different types and degrees of lung mobility it is generally possible to demonstrate the clinically important sign of *diminished or absent lung mobility*. The mobility of the lung border is diminished in—(1) *pulmonary emphysema* and in (2)

Fig. 127.—Method of apical percussion.

partial consolidations of the lung. Although the percussion-note may not be noticeably dulled if these consolidations be scattered, such a condition may be suspected from the immobility of the border. (3) *Firm pleuritic adhesions* between pulmonary and costal pleura also prevent mobility.

Some examiners attempt to demonstrate pleuritic adhesions of the lung edge by percussing below the border determined during quiet breathing while the patient breathes deeply. If the loudness of the note be much increased with inspiration, they then claim that the lung edges are freely mobile. This method of examination, according to the author's experience, often causes error. Even if the lung be quite adherent, the intensity of the note beneath the lung border is almost certain to increase during inspiration. Such an increase does not necessarily prove a descent of the boundary, but merely suggests a thickening or

an inflation of the lung edge. In other words, a greater accumulation of air at or near the pulmonary edge influences the note, because even with the lightest percussion it is not possible absolutely to localize the percussion stroke.

A much better method for demonstrating mobility of the pulmonary border is to determine the boundary in the position of extreme inspiration while the patient holds his breath, mark it on the chest, and then do the same during extreme expiration. The best method is to utilize, in addition, the passive excursion of the lung border by turning

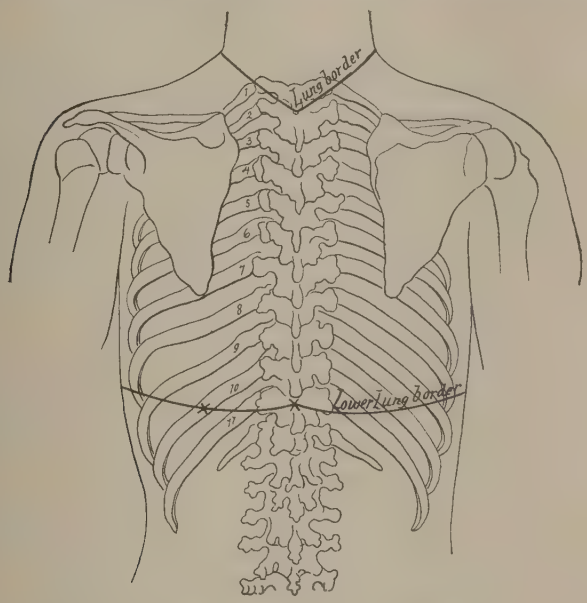


Fig. 128.—Normal percussion boundaries (from behind).

the patient to the opposite side from the one being examined, while he retains at the same time the position of deep inspiration, and in this way to accentuate the result. When so determined, the finding is especially trustworthy for the anterior and lateral boundaries.

ABNORMAL POSITION OF THE LUNG BOUNDARIES

Under pathologic conditions the lung boundaries may be extended as well as contracted.

Extension of the lung boundaries occurs in *emphysema,* where the lung-liver boundary may reach down to the eighth rib in the right mid-clavicular line, to the ninth or tenth rib in the axillary line, and to the twelfth vertebra behind in the posterior median line; in fact, quite to the inferior limit of the thorax. The emphysematous increase may sometimes be plainly demonstrated even at the lung apex, and over the superficial cardiac dulness, which may be either entirely or almost obliterated. Both the active and the passive mobility of the borders in

emphysema are diminished on account of the permanent inspiratory position of the diaphragm and a certain rigidity of the lung so characteristic of the disease. Emphysema is ordinarily developed upon both sides, and, as a rule, quite uniformly; but a partial emphysema does occur (perhaps incorrectly called *vicarious emphysema*), in which the changes are localized at the lung borders. Even in the common type of pulmonary emphysema the pulmonary distention is not always uniform. Percussion frequently shows that the emphysema is limited to the region over the heart, whereas the inferior lung border is not any lower than the normal. This is often seen in fat or dropsical individuals, apparently because the increased abdominal contents crowd the diaphragm upward.

In a similar manner the pulmonary boundaries are extended in attacks of *bronchial asthma* and in *obstructive bronchitis* because there is a greater resistance to the emptying (p. 96) than to the filling of the lungs (acute pulmonary distention). For analogous reasons, when a bronchus is narrowed, the affected pulmonary lobe is distended.

Certain chronic *cardiac affections*, particularly mitral lesions, lead to pulmonary distention, the lungs being permanently engorged with blood and in the condition of so-called cardiac lung rigidity; brown induration is usually present as well. The lungs in these cases resemble those of emphysema, since they are distended, their elasticity is partly lost, and they make but slight excursions.

However, only advanced cases of known induration can be distinguished by percussion.

The *acute congestion of failing compensation* can also frequently be recognized by extension of the lung boundaries and so can *pulmonary edema*, provided, of course, that the pulmonary edges in the latter condition still contain air.

The lung borders in *enteroptosis* (p. 253) are nearly always depressed.

Retraction of the lung boundaries results from the crowding of the lung edges by the neighboring parts. 1. The diaphragm will be pushed upward by all conditions which increase the intra-abdominal pressure, *e. g.*, *meteorism*, *ascites*, *abdominal tumors* (especially if situated at the convexity of the liver). The intrathoracic pressure will, therefore, approach more nearly that of the external air; so the lungs must be retracted, not only upward, but concentrically in all directions, from in front backward and toward the hilum, even enough to expose the heart to a considerable extent. 2. An *enlarged heart* (or a *pericardium filled with fluid*) can also crowd the lungs aside enough to increase the superficial cardiac dulness. (See Heart Percussion.) If such a crowding be very marked, the resulting intrathoracic pressure will elevate the inferior lung borders. 3. All processes associated with a pulmonary shrinking may occasion a retraction of the lung boundaries, *e. g.*, the *chronic forms of tuberculosis*, which produce a connective-tissue retraction of the lungs; and cases of *pleurisy* in which, after the absorption of the exudate, the expansion of the compressed portion of the lung is prevented by the formation of a firm connective-tissue coating. The shrinking usually proceeds concentrically in such conditions, so that the lungs are often retracted on all sides—that is, as much over the heart as at the inferior borders, and sometimes even at the upper borders, toward the hilum. Chronic tuberculosis frequently leads to a retraction of the pulmonary apex. Therefore the demonstration of a low position

of one superior lung border is of special importance for the early diagnosis of apical tuberculosis.

We must remember that the normal positions mentioned above are only averages, and that abnormally long or short chests would naturally modify the position of the lung borders in relation to ribs, although the condition could in no way be considered pathologic. Errors in this respect, especially in relation to the diagnosis of emphysema, frequently occur in practice. They cannot be avoided by definite rules, but only by practical experience and by the development of a geometric vision.

TOPOGRAPHIC PERCUSSION OF THE HEART

RÖNTGEN ORTHODIAGRAPHY OF THE HEART UNDER PHYSIOLOGIC AND PATHOLOGIC CONDITIONS: RESULTING CONCLUSIONS AS TO ITS SIZE AND RELATIVE POSITION

As we shall see, only certain limited, though practically important, conclusions regarding the size and position of the heart can be drawn from topographic percussion. Hence the importance of Röntgen orthodiagraphy, the elaboration of which we owe to Moritz, for it furnishes us with a means of studying normal and pathologic anatomy in the living subject, thus eliminating such changes as accompany death and the distortion necessarily entailed in postmortem examinations; and, in addition, it can be employed as a sort of control immediately after the other examination

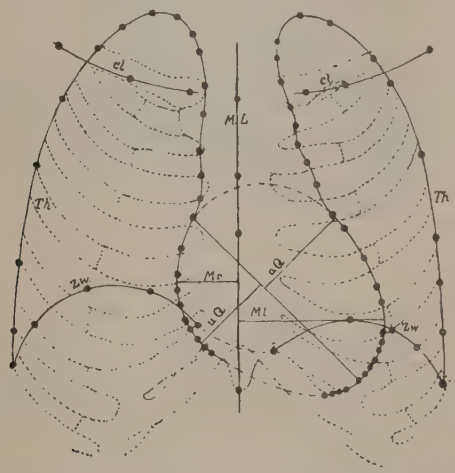


Fig. 129.—Orthodiagram of the stomach, lung area, and diaphragm of a normal man (one-fourth natural size) (Moritz): *Cl*, clavicle: *Ml*, median line; *Th*, thoracic wall; *Zw*, diaphragm; *Mr*, distance of the right border of the heart from the median line; *Ml*, distance of the left border of the heart from the median line; *uQ* and *oQ*, lower and upper transverse partial diameter of the heart. The latter are drawn perpendicular to the cardiac axis. *uQ* + *oQ*, the diameter representing the width of the heart.

methods. Röntgen orthodiagraphy presents the relations of size and position more accurately than Röntgen photography, because the former does not exhibit the shadows due to the divergent rays, which cause much distortion.

In Röntgen orthodiagraphy the *x*-ray tube moves in a plane which is parallel to the plane of the fluorescent screen. The projection point of the vertical rays on the screen is indicated by a rod which is attached to the *x*-ray tube, passes around the patient, and ends in a marking-point just in front of the screen. The apparatus is so constructed that, as the *x*-ray tube is moved about, the marking-point always touches the fluorescent screen at the place where the vertical rays are projected. In

this way the shadows cast by the bony landmarks and the more solid organs are outlined on tracing paper attached to the fluorescent screen or on the skin of the patient. As shown in the accompanying illustrations, numerous heavy dots mark the contours, and the outlines are completed by joining them.

One of Moritz's figures, an orthodiagram, showing the size and position of the normal heart, is reproduced here. (See Fig. 129, p. 229.) The oval heart shadow seems to be suspended within the thoracic skeleton by the cardiac hilum, which is composed of the mediastinum and its great vessels. Fig. 120, p. 218, a graphic representation of the organs in situ, should be compared to understand properly the significance of the individual parts of the shadow. Attention should be called to the fact that the right and left portions of the inferior borders of the heart are located with accuracy, despite the presence of the hepatic shadow. Mere percussion is not sufficient to do this except to a much more limited extent. The points of

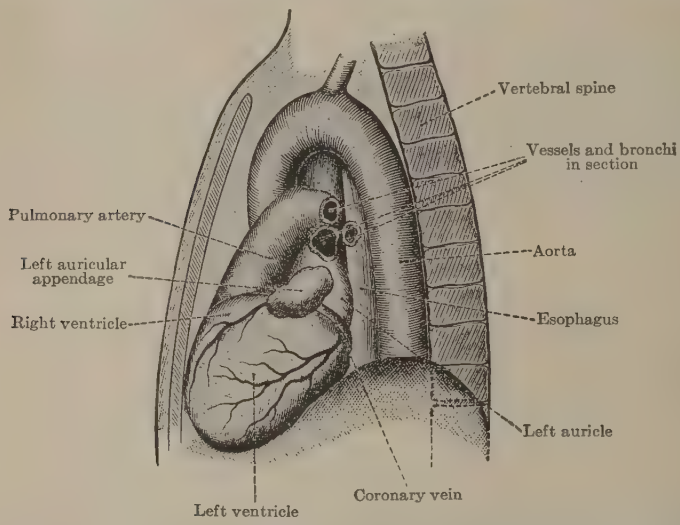


Fig. 130.—Schematic view of the cardiac region from the left, the lung having been removed (Moritz).

the lower parts actually determined orthodiagraphically are represented here and in the following orthodiagraphic figures by heavy dots. The meaning of the artificial lines used for measurements is indicated in the legend, and the manner in which they are drawn is apparent from the diagram. Fig. 130 is a schematic lateral view of the cardiac region. Fig. 131 is its Röntgen orthodiagram, the direction of the ray being from right to left.

Dietlen[1] gives the following figures for the measurements of an orthodiagram of a normal heart:

MEASUREMENT OF THE ORTHODIAGRAPHIC HEART SILHOUETTE IN HEALTHY ADULT MALES

(Abbreviations are explained in Fig. 129 and the following pages and in the foot-note upon page 236.)

Height cm.	Weight kg.	*Mr.* cm.	*Ml.* cm.	*Tr.* = *Mr.* + *Ml.* cm.	Length cm.	Width = *oQ* + *uQ* cm.	Area sq. cm.
145–154	mean 47	3.7	8.5	12.2	13.4	9.6	103
155–164	" 57	4.2	8.7	12.9	14.0	10.2	111
165–174	" 64	4.3	8.8	13.1	14.2	10.3	117
175–187	" 71	4.5	9.3	13.8	14.9	11.0	131

[1] Deut. Arch. f. klin. Med., 1906, vol. lxxxviii.

The cardiac measurements increase in proportion to the stature and weight of the individual, the influence of the latter being more important than that of the former. Dietlen found that the measurements were about 0.5 cm. smaller in women than in men of the same height and weight; that they were somewhat smaller in youths than in adults of the same height; and that they were greater in elderly individuals of middle age.

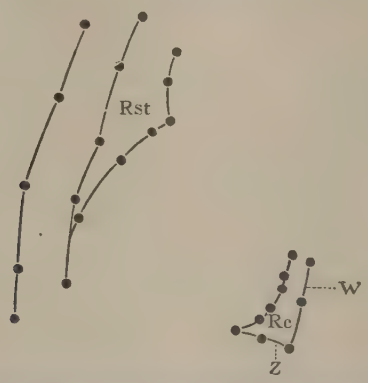


Fig. 131.—Orthodiagram of the thorax taken from the side (corresponding to Fig. 130), with well-developed retrosternal (*Rst.*) and retrocardiac (*Rc.*) spaces: *W*, anterior margin of the vertebral column; *Z*, diaphragm in position of expiration (one-third natural size).

Moritz[1] and Dietlen[2] have studied, with the assistance of this method, the changes in size and position of the heart under physiologic and pathologic conditions. A short résumé of their most important conclusions follows: In changing from the recumbent to the erect posture the heart sinks 2 to 4.5 cm. (Fig. 132). All the abdominal viscera, especially the liver with the diaphragm, participate in this descent. According to the author's percussion, however, and he believes that per-

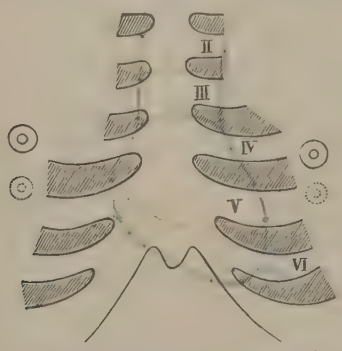


Fig. 132.—Orthodiagram of a normal heart. Red line, in horizontal position; blue line, in upright position (two-ninths normal size)(Moritz).

cussion can be relied on in this case (see p. 225), the shifting of the lung borders proceeds in the reverse direction. With the assumption of the erect posture the heart as it descends assumes a more vertical position, revolving on a sternovertebral axis, passing through the great vessels, so that the transverse diameter of the shadow is shortened by 2.5 cm. (Fig. 132). In fact, all its diameters are frequently slightly

[1] Deut. Arch. f. klin. Med., vol. lxxxi, p. 1 et seq.; vol. lxxxii, p. 1 et seq.; Zeit. f. klin. Med., vol. lix; Deut. Klinik, Methoden der Herzuntersuchung, 1906.

[2] Deut. Arch. f. klin. Med., vol. lxxxviii.

diminished. Moritz attributes these reduced measurements to an actual diminution of the size of the heart, due essentially to its decreased filling, dependent upon an increased accumulation of blood in the territory of the vena cava inferior.

When the patient lies on his side (Figs. 133 and 134), orthodiagraphy shows the same lateral displacement of the heart as does percussion. (See p. 240.)

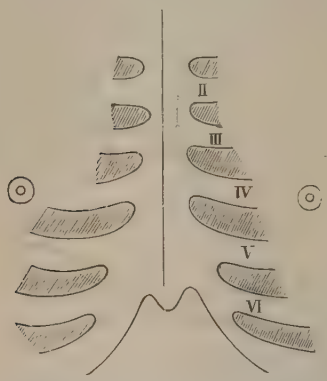


Fig. 133.—Orthodiagram of the normal heart (nineteen-year-old male). Red line, dorsal position; blue line, right lateral position (two-ninths natural size).

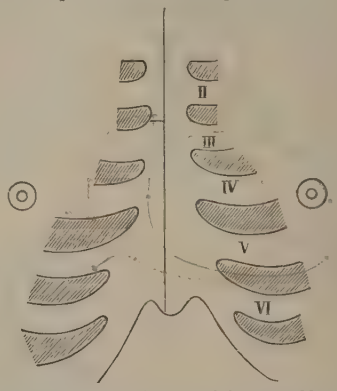


Fig. 134.—Orthodiagram of the normal heart (nineteen-year-old male). Red line, dorsal position; blue line, left lateral position (two-ninths natural size) (Moritz).

The position of the diaphragm in respiration has, as is to be expected, a decided influence on the position of the heart. With the aid of the orthodiagraph it is plainly demonstrated that the heart sinks with inspiration, and at the same time undergoes those changes in shape and size which have been described as characteristic of shifting from the horizontal to the vertical posture. Moreover (as, for example, in old age), a lower position of the diaphragm is associated with a corresponding lower

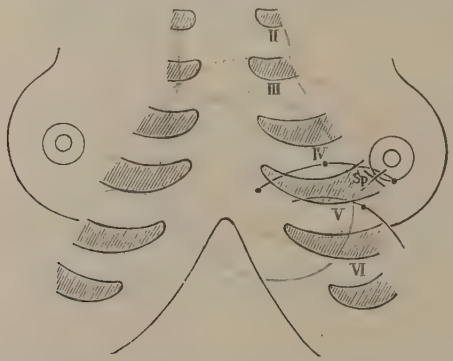


Fig. 135.—Red line, orthodiagram of a healthy girl's heart, age twenty; blue line, orthodiagram of a healthy man's heart, age thirty (two-ninths natural size).

position of the heart. Concerning the relations of the position of the diaphragm the reader should compare the notes upon orthodiagraphy of the diaphragm (p. 222). According to Dietlen, an orthodiagram shows that the heart is in general placed more horizontally when the diaphragm is low (except in emphysema and asthma, see below).

This writer found the heart-shadow about one intercostal space higher in females than in males (Fig. 135). He attributes this to the higher position of the diaphragm in women. (See p. 222.)

Moritz and Dietlen examined the heart in pathologic conditions, among others, in asthma and emphysema. In both the latter they found a narrow, vertically placed heart situated low down in the thorax. A similar finding is observed in pneumothorax and in healthy, slender young subjects of both sexes, especially in young girls. A tightly laced corset crowds the heart upward.

The excursion of the heart shadow between systole and diastole amounts to only a few millimeters. This explains why one cannot elicit a difference in percussion between the cardiac phases.

The apex impulse almost never corresponds to the position of the apex in the orthodiagram of the heart, but is usually about an intercostal space higher and nearer the median line. Dietlen explains this more median position of the apex impulse as follows:

At the apex the excursions of the heart wall are at a maximum, so that there is a distinct difference between the position of the heart, which corresponds to the movement of the cycle coinciding with the apex-beat, viz., systole, and that which corresponds to the shadow represented orthodiagraphically, viz., diastole. The author's objections to this explanation will be found below.

Dietlen explains the high position of the apex-beat in relation to the lower edge of the heart shadow by the fact that the latter coincides with the border of the right ventricle, while the former belongs to the left ventricle. The author believes that the apex impulse is so frequently situated nearer the median line than the left border of the cardiac orthodiagram essentially because the apex itself is covered by lung tissue, so that the outer portion of the apex impulse is inaccessible to palpation. Therefore, the apex impulse in the strictest sense, *i. e.*, the strongest pulsation within the left cardiac border, can be appreciated only when the heart is entirely, or almost entirely, exposed. In the last edition of this book the author described a similar discrepancy between the results of palpation and of percussion, so Dietlen is wrong in ascribing to the author the statement that the position of the apex impulse is identical with the left border of the heart. On the contrary, the author has maintained, on the evidence of percussion, that the apex impulse does not always coincide with the extreme left of the cardiac wall, though he acknowledges that he did not lay this down as an arbitrary rule.

The author prefers his own explanation of this peculiarity (overlapping lung) to that of Dietlen (difference in the systolic and diastolic position of the apex). Against the latter may be argued that the excursions of the heart boundaries in the region of the apex are very slight, as demonstrated by the orthodiagram, and that the apex impulse coincides with the closure time when the heart has not yet contracted. (See the section upon the Apex beat.) Moreover, it must be added that, in the cases where the apex impulse coincides with the external border of cardiac dulness, both these points not infrequently lie outside the orthodiagraphic projection of the heart shadow upon the anterior thoracic wall. The reason for this is, that if the heart apex lie at a point where the thoracic wall has already curved sharply backward from the frontal plane, the boundaries of the deep cardiac dulness naturally extend beyond, and the apex impulse lies outside of, the frontal projection of the heart, foreshortened in the orthodiagram upon the sharply bent thoracic surface (cardiac dulness larger than the heart; see p. 239).

NORMAL SUPERFICIAL AND NORMAL DEEP CARDIAC DULNESS

Superficial cardiac dulness is the dulled area which corresponds to the notch of the left lung about the heart (Figs. 125 and 136). Its extent really tells more about the position of the lung edge than about the size of the heart. Nevertheless, if the heart be enlarged or if the pericardium become distended with fluid, the edges of the lung will be pushed back and the superficial cardiac dulness be increased. Certain cautions are necessary to prevent mistakes in estimating the size of the heart or pericardium from the extent of this superficial cardiac dulness. For example, despite an enlarged heart, the superficial cardiac dulness is not necessarily increased in emphysema, nor need it be if the lung edges in the neighborhood of the heart be fixed by pleuritic adhesions. The deep dulness is more important in estimating the size of the heart and the contour of the pericardium. Deep cardiac dulness is never very intense, but is always modified (a so-called relative dulness).

The beginner often finds it very difficult to determine. The superficial cardiac dulness, on the contrary, is frequently absolute, and therefore easier for the beginner's ear to appreciate. Both varieties of dulness should, therefore, be mapped out upon the chest. The superficial often confirms the results of the deep percussion.

In estimating both superficial and deep dulness it is advisable to follow exactly the method described upon p. 210 et seq. The form and size of the superficial dulness, also called the small cardiac dulness, have already been described in the section on Topographic Percussion of the Lungs. (See Fig. 125, p. 223.) Fig. 136 represents the relations of the superficial and the deep or great cardiac dulness in the average healthy adult. The boundary of the latter runs from the upper edge of the third left rib nearly parallel to the border of the superficial

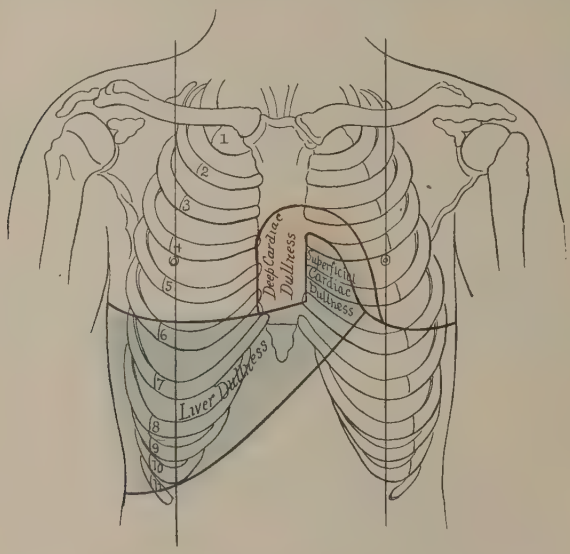


Fig. 136.—Superficial and deep cardiac dulness under normal conditions.

cardiac dulness, bends toward the left in a curve, with the convexity outward, becomes perpendicular slightly inside the midclavicular line, and ends near this point at the apex-beat. The heart is bounded below by the liver, so that the deep dulness throughout its whole extent (see Fig. 136), like the superficial, merges below into the hepatic dulness and cannot be differentiated from it. If tympanitic intestines overlap the liver or crowd it upward and to the right, superficial percussion will generally evoke a loud tympanitic note just below the heart. Fig. 140, p. 245, illustrates such a condition, although it should be noted that whereas in this figure the region of the heart apex seems to be entirely covered above, it can project beyond the lung edge below, in which case the inferior cardiac boundary exhibits throughout its entire extent the characteristics of a superficial dulness. This so-called "inferior cardiac boundary" will always be difficult to distinguish from the dulness of

the liver edge. Most writers limit the right boundary of the deep dulness at the left sternal border; nevertheless, according to the author's experience, the majority of healthy adults show a slight dulness up to or just beyond the right sternal border (Fig. 136).[1] But in many cases the whole extent of the sternum furnishes so resonant a note that the deep cardiac dulness is really limited by the left sternal border. (See Topographic Percussion of the Lungs.) These individual peculiarities depend upon the vibration of the sternum, upon the thickness of the layer of lung covering the heart, etc.; nevertheless the author regards it as the rule that the deep dulness can be traced as far as the right edge of the sternum and even 1½ cm. beyond. The reason other observers obtain different results, limiting the right edge of the deep cardiac dulness at the left edge of or in the middle of the sternum, is because they do not follow the methods for eliciting deep dulness which were described upon p. 210 et seq. In determining the upper borders of the deep dulness the sternum transmits the blow so deeply that a lighter percussion becomes necessary, even though deep dulness is to be elicited. It was established upon p. 211 that deep dulness should never be determined by very vigorous percussion.

The device to simplify cardiac percussion by having the patient bend over and assume the expiratory position is discussed under Active and Passive Mobility of the Superficial and Deep Cardiac Dulness.

To determine the deep cardiac dulness in women with well-developed breasts, the left breast should be lifted up and held away from the field of examination.

Percussion is not concerned with the excursions of the heart from diastole to systole. According to orthodiagraphic examinations, these excursions amount to but a few millimeters (see p. 233), and percussion is too inaccurate a method of examination to distinguish such differences, even if we disregard the difficulty of undertaking so fine a distinction within the cycle of a single cardiac revolution.

Variations of the thoracic dimensions in different individuals make the conclusions to be drawn from deep cardiac percussion still more doubtful. The heart boundaries are ordinarily mapped out in accordance with the orienting lines of the body, *e. g.*, the position of the left border of the heart in reference to the mammillary line. This sometimes leads to erroneous conclusions. Although, as a rule, the left border of the deep cardiac dulness lies somewhat inside the mammillary line, it is self-evident that if the mammillary line lie near the midline, even a normal heart would extend beyond it. Even the midclavicular line is not absolutely constant, because the length of the clavicle sometimes varies out of proportion to the breadth of the thorax. If the sternum be broad, a dulness beyond the right sternal edge is more significant than if it be narrow. Hence the importance of the absolute size of the cardiac dulness.

To estimate this, the author recommends determining, in as close accord with the normal orthodiagraphic measurements as possible, the distances from the midsternal line to the extreme left and to the extreme right limits of the deep cardiac dulness, as well as the distance from the highest point of the deep cardiac dulness upon the middle of the sternum to the apex impulse or, if it be possible to percuss out the inferior cardiac boundary (see p. 234), to the lowest point of the latter.

[1] [I determined the right border of deep cardiac dulness in 60 boys between the ages of fifteen and twenty-one. It extended to or beyond the right sternal edge in over 70 per cent. of them.—Ed.]

Dietlen's table (p. 230) furnishes approximately average figures for these distances: *Mr*, *Ml* (width to the right and left of the median line), and *L* (length).

According to the author's experience these orthodiagraphic normal measurements correspond sufficiently accurately to those mapped out in the figure representing the results of deep cardiac percussion. The opportunity to compare the measurements obtained during life with those of the anatomic size and position of diseased hearts in pathologic cases at autopsy clearly proves that deep percussion is a very trustworthy method, provided, of course, the examiner be sufficiently skilled in the technic.

The statements presented here differ in several particulars from those advanced recently by Moritz and Dietlen,[1] which were based upon their examinations controlled by the corresponding orthodiagram. The main differences are, therefore, summarized in what follows. They base their examinations upon orthodiagraphic heart figures (see p. 229 et seq.), and believe that the results of their percussion coincide almost perfectly. They accordingly represent in their articles figures of cardiac dulness which correspond more or less accurately with the real orthodiagraphic heart silhouettes.

Thus, their figures are depicted, for the most part, as open above, with the lateral borders of the heart proper prolonged in broken curved lines corresponding to the boundary of the orthodiagraphic shadow of the hilum of the heart (see Fig. 129, p. 229), and running parallel to the sternum. In many cases, to be sure, these mediastinal boundaries are not continued very far upward; but stress is laid upon percussing out the right "heart vessel angle," because the latter forms the basis for the linear measurement of the heart dulness.[2] In many cases between the two heart vessel angles a horizontal upper cardiac boundary, represented by the dotted line in Fig. 129, p. 229, can be distinguished from the "hilum dulness." Moritz and Dietlen further find, corresponding to their orthodiagraphic heart figure, and differing from the heart figure as represented by the author (Fig. 136, p. 234), that the right lateral deep cardiac border forms an acute angle with the right inferior lung border (Fig. 129, p 229). The third difference is that Moritz and Dietlen "in most cases" map out the inferior cardiac border in the region of the apex by percussion and quite in accord with their orthodiagraphic results, whereas the author has explained that it is impossible to percuss out the inferior heart border in the region of the apex except in the cases which present a considerable portion of the inferior cardiac border free from the left lobe of the liver.

Corresponding to the Moritz-Dietlen pictures, the author agrees that from the heart upward the sternum, together with a very narrow zone outside of and along each sternal edge, does furnish to *moderate percussion* a note which is slightly dull compared to that obtained further to the sides. This dulness can be accredited, perhaps in part, to the contents of the anterior mediastinum, *i. e.*, the heart hilum, but the author does not believe that it is correct, at least under normal conditions, to identify this dulness with the orthodiagraphic heart hilum. Now the sternum, especially its superior portion, is fixed by a firm buttress, the short immobile first rib, so that the percussion-note over it and in its immediate vicinity must be dulled. Who, therefore, can distinguish how much of such a dulness is produced by this peculiar conformation of the chest-wall and how much by the great vessels? For normally the dulness is rather slight and indistinct. In addition to this, the actual topographic percussion of organs is scarcely feasible here when we consider that the great vessels run directly backward and are hidden under quite thick layers of lung which almost meet in the median line, as is shown by Fig. 120, p. 218. Under pathologic conditions, such as dilatation of the arch of the aorta or dislocation of the mediastinum by pleural exudate, etc., percussion and usually even superficial percussion, can bring out the dulness because the lungs are forced apart. This zone of dulness has already been described in earlier editions of this work, and in this edition it will be discussed further

[1] Moritz, Arch. f. klin. Med., vol. lxxxviii, 1906; Dietlen, ibid.; also Dietlen, Methods of Examination of the Heart, Deut. Klinik, 1906.

[2] They draw the long diameter of the heart figure (see Fig. 129, p. 229) from the right "heart-vessel angle" (heart-cava angle) to the point of the figure farthest downward and to the left, and they represent the width as the sum of the two partial diameters perpendicular to this diameter.

under the special discussion of the results of percussion. As the author does not consider that this mediastinal dulness which exists under normal conditions can be utilized for diagnosis, he naturally cannot accede to the Moritz-Dietlen proposition to attribute topographic value to the angle which they outline by percussion between the lateral heart borders and the border of the heart hilum, so as to be able to measure the heart exactly as in the orthodiagram, Fig. 129, p. 229, nor can he, as an instance in point, utilize the right "heart-vessel angle" (heart-cava angle) as a starting-point for estimating the length of the heart. Neither can he comprehend how these writers can prolong the heart dulness into the hilum dulness, as mentioned above, and then, despite such a continuity (see the plates in Dietlen's work), percuss out the heart hilum from the upper cardiac border.

The author also takes exception to the next two deviations from the usual interpretation which these recent studies have advanced, viz., that percussion brings out the existence of an acute instead of an obtuse or at most a right pulmonary cardiac angle between the right inferior lung border and the right border of deep cardiac dulness. Viewed in the frontal plane, this angle is plainly acute, as is evident from the consideration of both anatomic and orthodiagraphic studies. (See Figs. 120, p. 218, 129, p. 229.) Viewed, however, in their three dimensions, this apparent discrepancy is explained; because if one percuss just to the right of the right border of deep cardiac dulness in continually lower horizontal levels, the dulling influence of the liver convexity entering the area of the percussion blow is more and more apparent, the lower one percusses until the acute angle becomes plainly blunt or obtuse. (See p. 210 et seq., The Laws of Deep Percussion.) Another objection is that this cardiohepatic angle frequently lies beneath the sternum in its whole extent, and such a position is inaccessible to deep percussion, since pronounced lateral vibrations are transmitted too widely over the sternal surface to render an accurate outline possible. Normally, therefore, according to the author, the acute heart-liver angle evident in the orthodiagram cannot be demonstrated by percussion. Under pathologic conditions, on the contrary, the oblique inclination of the right heart border outlined upon the right thoracic wall may be so pronounced that even an area of superficial dulness can be demonstrated there, as in Fig. 142, p. 247.

The third point in which the author differs from the views of Moritz and Dietlen concerns the interpretation of the results of percussing the inferior heart border in the region of the apex. As already explained (see p. 234), if the left lobe of the liver be slightly pushed to the right, the author believes this boundary accessible to percussion, but this is rarely the case. They even claim to be able to differentiate by percussion the lower heart border from the left lobe of the liver (Moritz, Deut. Klinik, *loc. cit.*, p. 523; Dietlen, *loc. cit.*, p. 293). From the standpoint of physics this seems quite incomprehensible. It is impossible to percuss the boundaries between two solid organs.

These two writers next endeavor to support their entire presentation by the accurate conformity of the results of their percussion with orthodiagraphy. They attempt to demonstrate statistically such an accord by tabulating the percentage of cases in which the different orthodiagraphic diameters of the heart shadows (see Fig. 129, p. 229) were correctly percussed, and by comparing the average error of percussion with the orthodiagram taken immediately afterward. They considered the diameters correctly percussed if the difference from the figures derived from the orthodiagram did not exceed 0.5 cm. They designated as the total linear error of each percussion of the entire heart the sum of the linear errors in excess of 0.5 cm., and evidently this total was constructed without regard to the character of the error. Employing this method of control, their results were excellent. A verdict of correspondence of percussion with orthodiagraphic examinations based upon such results seems, however, somewhat too optimistic. Statistics in such comparisons have the peculiarity of confusing rather than elucidating the relations. The main question is apparently not in what percentage of the cases the different heart diameters were found to be correct, *i. e.*, in accordance with the criterion assumed, to vary less than 0.5 cm. from the corresponding orthodiagram; nor is it the main interest to know how great the average linear total errors were in the cases examined, but the cardinal point is to know how large the maximum error of percussion may be. Before the introduction of orthodiagraphy we already knew that the results of deep cardiac percussion conform accurately enough with the postmortem findings to warrant our trust in this method of examination, and this conformity is upheld by the experience at the Bern clinic year in and year out. It is, on the contrary, much more important to know to how great a degree one can err with percussion. Statements in regard to the possible maximum error, to be sure, do appear in the above-named studies; but in their conclusions too little importance is attributed to them. The great errors are

the sources of erroneous percussion diagnoses. Now it is evident that in percussing the different diameters of a heart one does not commit great errors throughout. Let us assume that for one diameter we have committed a great, perhaps the maximum, error possible, although most of the other diameters have been correctly percussed. Under some circumstances so great a mistake of even a single diameter involves an entirely incorrect percussion diagnosis, and yet if all the diameters except one were correctly estimated, the result would seem to be quite insignificant, provided we estimated the heart percussion in accordance with the above-described summation of the total linear errors of percussion obtained by adding the total errors of the different diameters. We should then arrive at the erroneous conclusion that percussion in this case had succeeded well. If, however, we acknowledge that these linear totals in cardiac percussion in reality depend upon a mistake in a single diameter, the judgment of the results of percussion will naturally be much less favorable. The question of the reliability of percussion is obscured by this manner of reckoning. The obscurity is deepened when an attempt is made to determine the mean linear totals of error for definite age subdivisions. It is perfectly conceivable that judgment of the reliability of percussion would be still more favorable by continually multiplying the number of cases used for the estimation because the gross errors would become more and more insignificant compared to the larger number of approximately accurate estimations. But how can a clinician be satisfied that percussion becomes more accurate when it is simply a theoretic improvement which depends entirely upon an increase in the amount of statistical material and when practically errors as great as 2.5 cm. (Moritz) may occur in an individual case, although the mass of statistics seem to prove that such errors are unimportant and negligible? Besides which, errors of percussion which do not exceed 0.5 cm. have been disregarded in each instance and considered as equal to zero, although it would be mathematically correct to consider such errors in summing up the total linear error.

The method of deep percussion should not be balanced in the scales of statistics, especially if such statistics be derived from approximately normal cases. The actual valuation of percussion must be determined from pathologic cases submitted to the control of either anatomic or orthodiagraphic examinations. Autosuggestion, which must play some part in normal cases, is thus excluded. The two writers admit that their results were less trustworthy in pathologic cases.

Unfortunately, even these latest studies cannot alter the author's former opinion of the reliability of deep percussion of the heart. Moritz's and Dietlen's actual findings are in accord with this opinion, although their conclusions are at variance. Deep percussion of the heart supplies results approximating the actual condition, *i. e.*, the anatomic position or the orthodiagraphic projection; but under certain circumstances these results may be accompanied by grave errors as to the size of the cardiac dulness. No statistics can bridge over this gap in percussion,—a fault shared by every other clinical method of examination,—but we must depend only upon an increasing experience in the source of error which permits anticipating it in individual cases and recognizing the cases in which we can make use of percussion results only with reserve.

It is, therefore, important to study briefly these sources of error. Instances in point are abnormal overlapping of the heart by the lungs and abnormal conditions of the thoracic wall. The existence of the former abnormality may, in some cases, prevent the determination of any deep cardiac dulness, and in others, decidedly diminish it. Under these circumstances, which one can usually recognize by the peculiarity of the superficial dulness, it is a good plan to accentuate the percussion stroke and thereby force its sphere of action deeper. But such a plan has its limitations, for in spite of every caution (light application of the plexímeter), with too vigorous percussion it is not always possible to hinder the transmission of the percussion blow too widely over the body surface and so prevent the outlining of deep bor-

ders. The condition and the shape of the thoracic surface can make cardiac percussion more or less deceptive or falsify its results. Well-developed breasts or the fatty tissue of a stout man often render accurate percussion impossible. Here, too, by increasing the strength of the percussion blow, we may attempt to force its sphere of action deeper, but this device succeeds only up to a certain extent, for the same reason as mentioned just above. Certain deformities in the thorax in the neighborhood of the heart will naturally increase the difficulty of percussing the deep cardiac dulness. The existence of a so-called "heart hump" (see p. 34), dependent upon an enlargement of the heart, is another example. So are rachitic thoraces, because, as we shall recognize later under comparative percussion, very pronounced convexity of the chest walls dulls the percussion-note. (See p. 259.) An abnormal rigidity of the bony thorax will also present an obstacle to percussing the deep borders because the inflexibility naturally favors the lateral action of the percussion blow.

In conclusion, especial attention should be paid to the peculiar relations of size of the deep cardiac dulness which arise to a certain degree from purely geometric causes, when the left cardiac border projects beyond the sharp curve of the thoracic wall. This difficulty occurs

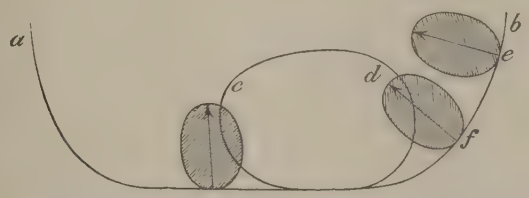


Fig. 137.—Relation of the size of the deep cardiac dulness in small children. The border of the maximum deep cardiac dulness comes to *f*, situated at the sharp convexity of the thoracic wall. As a result, the cardiac dulness seems much larger than is the heart or its orthodiagraphic frontal projection.

—(1) When the sphere of action of the percussion stroke is large in proportion to the size of the chest (as in small children); (2) when the heart is decidedly enlarged to the left, so that it projects into the lateral thoracic region, and finally (3) when the thoracic cross-section is more rounded or oval in shape, with a longer anteroposterior than transverse diameter. Such relations are well represented in the accompanying figure of a child's thorax.

The size of the dulness bears no relation to a frontal projection of the heart, but extends beyond it. Now, since the thickness of the lung covering at the border is unknown, it is not possible to estimate the actual size of the frontal projection of the heart. But even such cases need not cause mistakes in estimating the size of the heart, provided one always bears in mind the geometric relationship and has collected sufficient experience in regard to the disproportionate size of the deep cardiac dulness in normal children and in cases where the heart (the apex-beat) reaches well around into the lateral region of the thorax.

These are all examples of conditions in which uncertainty of the percussion is unavoidable, and in which the most accurate percussion represents the boundaries as too large or too small as contrasted with the frontal projection of the organ. None of the new modifications of

the methods of percussion for which so much has been claimed can overcome these difficulties, because none of them offers anything actually new. The clinician's task is to guard against drawing false conclusions from such percussion results, and to learn in what cases the results of deep percussion are and are not reliable. The great secret of the art of percussion consists in considering the results only as one sign and in critically examining these results before they are employed in diagnosis. Then we need not be deceived by deep percussion of the heart, even if we do denounce the reported practically complete conformity with orthodiagraphy.

ACTIVE AND PASSIVE MOBILITY OF THE SUPERFICIAL AND DEEP CARDIAC DULNESS

The heart borders, like those of the lungs, change their position actively with respiration and passively with change of the patient's position. Active mobility concerns both the respiratory overlapping of the heart by the lung edges and the movement of the diaphragm, and with it of the heart, while passive mobility influences the displacement of the lung borders and the accompanying position of the heart. The orthodiagraphic examinations (see p. 229 et seq.) furnish the most valuable information in regard to the displacement of the diaphragm and the heart.

The boundaries described above are estimated during quiet breathing in the dorsal decubitus. Deep inspiration diminishes the size of the superficial cardiac dulness more or less decidedly, or even obliterates it. Forced expiration produces the opposite effect, and in rare cases the right edge of the lungs retreats so far that a superficial dulness appears to the right of the right sternal edge. Inspiration depresses the deep cardiac dulness from 2 to 4 cm., usually narrows it, and makes its left border steeper. Therefore percussion during forced expiration (without exerting abdominal pressure) will sometimes reveal the true size of a heart which is extensively covered by the lungs. Moritz and Dietlen's orthodiagraphic examinations show that in this experiment the right border retains its position while the left border moves upward and outward. This must naturally be considered in estimating the significance of the finding.

In the left lateral posture the heart falls to the left and displaces the anterior edge of the left lung. The anterior edge of the right lung is only exceptionally found beyond the left sternal edge, because its excursion is normally limited by the line of the pleura beneath the sternum. (See Fig. 120.) Therefore in left lateral positions both the superficial and the deep cardiac dulness are increased to the left.

In right lateral positions the opposite displacement occurs. Both the deep and the superficial dulness will reach beyond the right of the sternum, while the superficial dulness to the left of the sternum may entirely disappear. Moritz' orthodiagraphic examinations[1] confirm these findings in the lateral posture completely. (See Figs. 133 and 134, p. 232.)

Changing from the recumbent to the sitting posture does not produce any constant change in the form or size of the cardiac dulness. The change in shape and position of the heart demonstrated by the

[1] Deut. Klinik, Methoden der Herzuntersuchung, 1906, Figs. 50 and 51, p. 504.

orthodiagram (see p. 231) can sometimes be elicited by percussion (depression, diminution of the size and especially narrowing of the deep cardiac dulness in the sitting posture). Both the superficial and the deep dulness may, on the contrary, seem somewhat more intense in the upright posture. If the patient bend forward, both are increased, because the heart pushes the lungs aside, approximating itself more completely to the anterior thoracic wall. Where emphysema or thick thoracic walls obscure the percussion in the recumbent posture, sitting up and bending forward may be helpful. To prevent mistakes the patient must be careful not to bend sidewise or twist his back, for we must remember that in such a position a normal heart will furnish a broader and more intense dulness.

The absolute measurements of the mobility of the superficial and the deep cardiac dulness vary so much with the individual that the figures would be superfluous.

PATHOLOGIC CHANGES IN THE SUPERFICIAL AND DEEP CARDIAC DULNESS

Diminution and Disappearance of the Superficial and Deep Cardiac Dulness

In *advanced emphysema, in left-sided pneumothorax*, in *pneumopericardium*, and in *precordial emphysema* both the superficial and the deep cardiac dulness may be either diminished or entirely disappear. The cardiac atrophy which is sometimes observed at the autopsy table is too slight to be recognized by percussion. *Emphysema* also causes an especially low position of the cardiac dulness, on account of the deep position of the diaphragm and because the heart is covered by the lungs. Frequently no deep cardiac dulness can be made out, and the superficial, if present, may appear only at the fifth or even the sixth rib. In interpreting the relations it should be remembered that orthodiagraphy has established that in emphysema the heart is situated low down and lies vertically, so that the frontal projection appears narrowed. (See p. 233.) In *left-sided pneumothorax* we should expect that at least a part of the superficial cardiac dulness would persist, because the normal division line of the pleura, which would divide the superficial cardiac dulness in half, is shifted (Fig. 120). As a matter of fact, however, left pneumothorax almost always dislocates the heart, the division line, and with it the mediastinum, so far to the right that the superficial cardiac dulness to the left of the sternum may entirely disappear. In *right-sided pneumothorax* (Fig. 135) the air resonance may overlap the left edge of the sternum, in consequence of the mediastinum being pushed to the left, so that the superficial cardiac dulness will appear to be narrowed from the right. The demonstration of the dislocation of the heart as a whole (p. 249) will explain this condition. Percussion elicits an abnormally resonant metallic note (often tympanitic) over the area of cardiac dulness in *pneumopericardium* and *precordial emphysema*. The pericardial sac in the former ordinarily contains fluid as well as air; this becomes evident when the patient sits up, for the lower portion of the abnormally resonant area becomes dull, the fluid following the laws of gravity. (The auscultatory signs will be mentioned later.)

With marked gaseous distention of the intestine or of the stomach, even careful percussion may elicit a tympanitic note over the area of superficial cardiac dulness,

because the vibrations are transmitted to the abdominal contents. But very gentle percussion, in which the pleximeter is applied only by its own weight, and perhaps best with the patient bending forward, will probably enable us to demonstrate the superficial cardiac dulness, and so to differentiate tympanites from the overlapping of the heart by air-containing tissue. A deep cardiac dulness in such cases is difficult, if not impossible, to obtain.

Enlargement of the Superficial and Deep Cardiac Dulness

Enlargement of the Cardiac Dulness from Abnormalities of the Lung Borders.—Both the superficial and the deep cardiac dulness will be increased if the heart push back the anterior lung boundary, or if some anatomic process in the latter (consolidation or atelectasis) add a dull tone of its own to the cardiac dulness. The increase of cardiac dulness does not then depend upon any alteration of the heart's size. Such conditions can be properly interpreted only by carefully considering the entire clinical picture, and by making use of other methods of examination. The most frequent examples are *pulmonary contraction* and the *concentric retraction of the lung*, or an upward dislocation of the diaphragm from marked ascites, meteorism, and the like. (See p. 228.) If the diaphragm be crowded upward, further evidence should be obtained before attributing an increase in the cardiac dulness to an enlargement of the heart.

The increase of the mediastinal fat described by von Hampeln can simulate an enlargement of the heart upward.

Increase of the Cardiac Dulness from Actual Increase of the Size of the Heart or of the Pericardial Contents.—Here the superficial and the deep cardiac dulness are generally increased correspondingly unless an emphysema or adhesions of the pulmonary border complicate the picture (p. 233). In the event of such a complication the superficial cardiac dulness may be much less enlarged than the deep; both may remain small, or may even be absent, on account of the marked covering of the heart. In this way even considerable cardiac enlargement might escape clinical demonstration. The relation of the lungs in other places (inferior pulmonary edge) ordinarily facilitates the diagnosis of these conditions and so prevents the error of deciding that the heart is not enlarged from the lack of an increased cardiac dulness.

The superficial cardiac dulness is very important in demonstrating cardiac enlargement; because the beginner finds it much easier to estimate than the deep dulness; because there is less chance for a subjective variation; and because in decided cardiac enlargement or increase of pericardial contents on account of the considerable lung retraction the entire cardiac dulness frequently becomes superficial.

Actual Enlargement of the Heart.—The heart is pathologically enlarged both by hypertrophy of its walls and by dilatation of its cavities. The extent of the former enlargement must, of course, be limited. The latter will be much greater and more easily recognized. If, while the chambers of a heart retain their normal size, its walls increase about 0.5 cm. in thickness from simple hypertrophy, a difference of only 1 cm. in the width of the heart would result. Now, as a matter of fact, we cannot percuss accurately enough surely to appreciate 1 or 2 cm. increase in cardiac size, nor do we practically ever see post-

mortem as much hypertrophy as 0.5 cm. unless complicated with dilatation. Evidently, then, any enlargement of cardiac dulness which can be demonstrated by percussion must depend upon the dilatation of the cavities, whether there be a coexisting hypertrophy or not.

An appreciable enlargement of cardiac dulness due to a pure hypertrophy of the heart, *i. e.*, one unassociated with dilatation, is, however, sometimes observed in very rare cases, particularly in chronic nephritis. In such cases a diagnosis of pure hypertrophy must be supported by other examination methods (increased force of apex-beat, persistent high-tension pulse, persistently elevated blood-pressure, and accentuated second tone (see below).

The cardiac dulness may be increased in all directions or only in one direction. We naturally attribute a dislocation of the left border

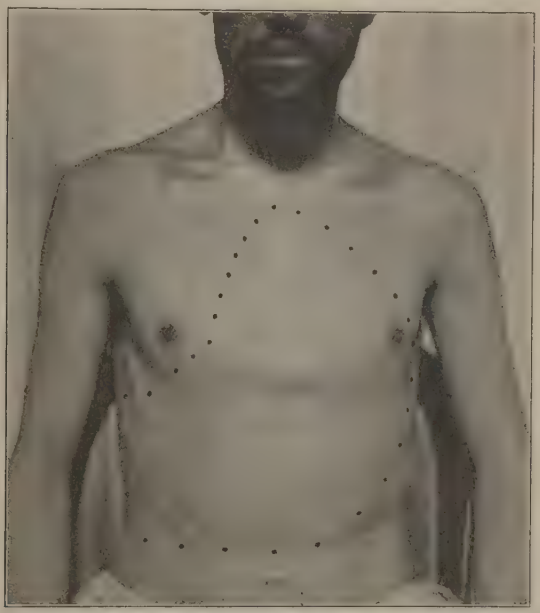


Fig. 138.—Precordial bulging: Enlarged heart and liver; double mitral lesion; percussion boundaries outlined by dotted lines. This picture does not bring out the marked precordial bulging which was very evident in looking at the patient. The width of the cardiac dulness at the nipple-line was 21 cm. (New York City Hospital).

of cardiac dulness to the left to a dilatation of the left ventricle; a dislocation of the right border to the right, to a dilatation of the right ventricle; an increase upward, to a dilatation of the auricles or of the great vessels. But the autopsy table has shown so many exceptions that these conclusions are by no means sure, *e. g.*, marked dilatation of the left ventricle may increase the cardiac dulness upward without there being any dilatation of the auricles or of the great vessels; because if the ventricle be dilated, the oblique position of the heart pushes the dulness upward. The clinical findings might very often induce us to assume a dilatation of the left ventricle when the dulness, as a matter of fact, depends only upon a dilatation of the right ventricle, or vice versâ;

or, again, to assume that only one ventricle is enlarged, whereas the autopsy shows that both share equally in the enlargement. The reason of this is that any dilatation of one chamber of the heart must secondarily dislocate the entire heart. Thus, dilatation of the right ventricle increases the dulness not only to the right, but often to the left, pushing the left ventricle in that direction. The position of the mediastinum is a factor in the difference of pressure at either side, *i. e.*, in the two pleural cavities, so that the actual position of a heart with dilated cavities is a complicated result of its own enlargement and of the difference of pressure at the two sides of the mediastinum, which difference is equalized by a dislocation of the mediastinum together with the heart. To make the matter still more complicated, the resistance to

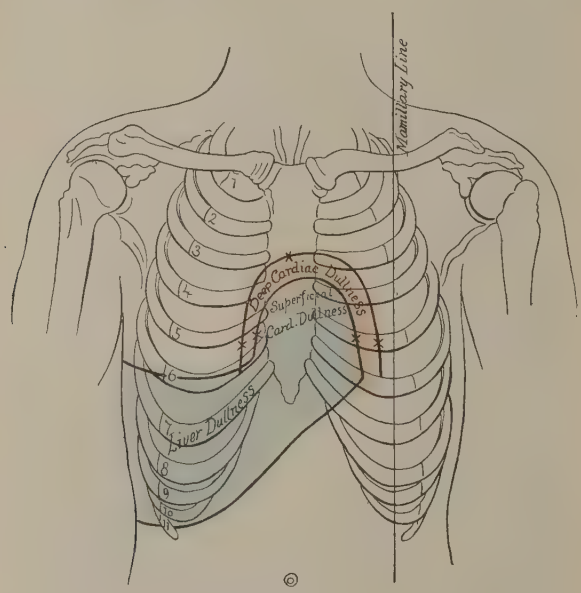


Fig. 139.—Cardiac dulness with dilatation of the right ventricle: dulness is especially increased to the right.

cardiac dislocation is by no means equal in all cases. Great differences are caused by the varying resistance of the mediastinum, by the varying amount of depression of the convexity of the diaphragm, and by individual variations of the prolongations of the pericardium upon the great vessel trunks. The existence of such differences is plainly proved by the different dislocations of the heart from causes acting outside of it (pleural exudates).

It is generally more difficult to demonstrate enlargements of the right heart by percussion than those of the left, because, on account of the notch in the left lung, the left heart is more accessible to percussion than the right, which is covered more completely by lung and by the sternum. Besides, the right ventricle (Fig. 120) rests upon the convexity of the diaphragm, so that if that chamber dilate, the heart

will have the tendency to find the necessary space in the left thoracic cavity because the arch of the diaphragm would present too great a hindrance to its enlarging to the right. Hence a moderate dilatation of the right ventricle often produces only a dislocation of the left cardiac boundary; while it requires a very considerable dilatation of the right ventricle to increase the dulness to the right of the sternum. The most familiar example of this is the displacement of the apex-beat to the left in pure mitral stenosis, where the left ventricle is certainly not dilated. Sometimes, however, the enlargement of the right ventricle (Fig. 139) can be definitely demonstrated to the right. In most of these cases the right auricle takes a prominent share in the enlargement of the right heart, and this is perfectly comprehensible if we remember (see Fig. 120,

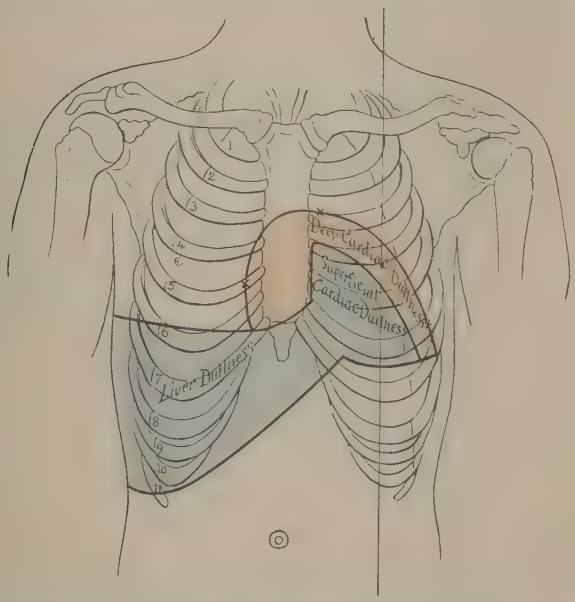


Fig. 140.—Cardiac dulness with dilatation of the left ventricle.

p. 218) that the right border of the heart is entirely formed by the right auricle.

So many exceptions make it clear that a diagnosis of the enlargement of a certain cavity cannot be determined from the direction of the increase of cardiac dulness without the general clinical picture and without other methods of examination. The position of the apex-beat, as we shall see below, is perhaps as helpful as anything. Figs. 139 and 140 show typical examples of the position of cardiac dulness in dilatation of the right and of the left ventricle.

Enlargement of the cardiac dulness upward may be due to dilatation of the ventricles, of the auricles, or of the great vessels. Percussion will frequently differentiate the latter two from the former. If the increase of the dulness upward be very pronounced (*i. e.*, in proportion to

the lateral enlargement), or if it assume the form of a projection from, or an appendage to, the ordinary area of cardiac dulness, it is to be referred to dilatation of the auricles or great vessels.

Figs. 141, 142, 143 (examples in point and the representation of the results of percussion in actual cardiac cases) support our contention that such figures are not stereotyped patterns, but correspond to the authentic findings in genuine heart disease. They show quite as characteristic shapes illustrating individual abnormalities as the orthodiagraphic imitation obtained by percussion which this modern method has so suggestively presented as substitutes. (See p. 236 et seq.) The diagnosis of left auricular dilatation and uncovering of the pulmonary artery can be made without question by comparing, in F g. 141, the striking extent, intensity, and superficiality of the dulness and its

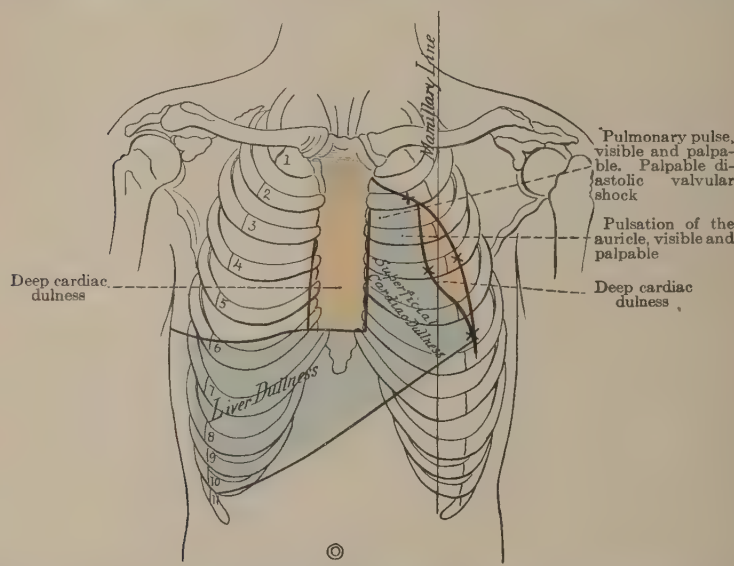


Fig. 141.—Dilatation of the left auricle and left ventricle, with an exposure of the pulmonary artery, in a case of mitral insufficiency.

peculiar projection upward, with the moderate increase of the cardiac dulness to the left, and also by noting the results of palpation appended to the chart. Similarly, Fig. 142 represents an enlargement of the right auricle and Fig. 143, one of the aorta. The three charts represent another important point in cardiac percussion, viz., the relation of the superficial to the deep dulness in enlargement of the heart. Figs. 139 and 140 show an enlargement outward, with the borders of superficial and deep dulness practically parallel to each other, so that, as under normal conditions, the superficial dulness is entirely surrounded (except below) by a strip of relative dulness. This illustrates a reasonably frequent occurrence; but quite as often with pronounced enlargement of the heart the relations represented in Fig. 141 appear. Here, at many points (in this figure above and near the apex-beat) or throughout

the entire extent of the heart the borders of the superficial and of the deep dulness merge so that there is only a superficial dulness. It results from the enlarged heart crowding back the lung edges, so that the entire heart lies directly against the thorax, and naturally furnishes only a superficial dulness. In Fig. 141 the left auricle has pushed the border of the lung so far aside that this chamber and the pulmonary artery both lie close against the chest-wall; while the less markedly dilated left ventricle is still partly covered by the lung; hence, outside of the superficial dulness, a slight relative or deep dulness exists.

Fig. 142 represents a marked dilatation of the right auricle and right ventricle in tricuspid insufficiency. Here again the lungs are pushed so far aside that the entire dulness is superficial, and the left edge and

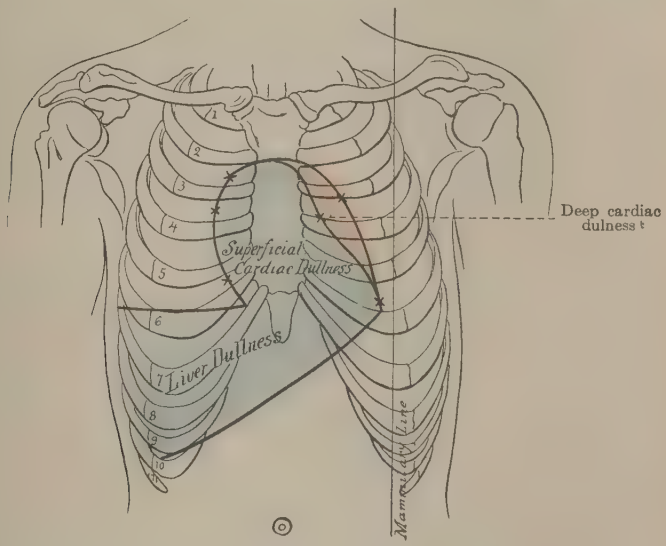


Fig. 142.—Dilatation of the right auricle and right ventricle in a case of tricuspid insufficiency.

the apex of the heart lie perfectly free. Above and to the left a small zone of relative dulness remains.

It can be seen in this figure, just as in Fig. 139, that the superficial dulness includes all the lower part of the sternum. Hence the dulness can be well defined above, although normally it is difficult to determine by percussion the solid from the air-containing parts (see p. 224) beneath the sternum.

From the bulging of the cardiac dulness upward, as in Figs. 141 and 142, the percussion results alone are not always sufficient to decide whether the auricles or the great arteries are responsible for the enlargement. The other conditions, especially the kind of pulsation over the area, will then assist in settling the diagnosis. (See Palpation and Inspection of the Heart Region.) The percussion results in Fig. 143 are, however, sufficiently characteristic to justify the diagnosis of a dilatation of the aorta.

Fluid Effusion in the Pericardium.—When fluid accumulates in the pericardium, whether as a result of general dropsy or of inflammation of the serous membrane, its cavity becomes more and more distended and the edges of the lung are pushed aside, just as by the enlarged heart. If the pericardium lie against the thorax wall, percussion elicits a superficial (often absolute) dulness; while where it is still covered by the lungs the dulness will only be relative, and the superficial and deep dulness will run concentrically. If the distention of the pericardium be very marked, the lungs will be pushed aside and the entire dulness may be superficial. The form and the position of the cardiac dulness enlarged by pericardial effusions are, from the anatomic conditions, generally very characteristic. (See the subsequent charts in the section, Diagnosis of the Different Valvular Lesions.) The specific

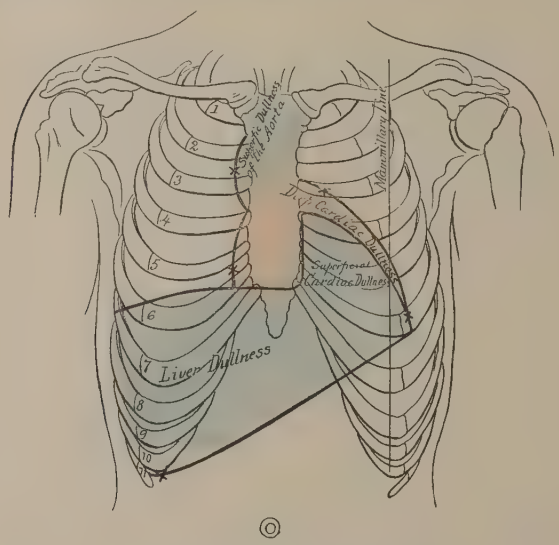


Fig. 143.—Cardiac percussion results in a case of diffuse dilatation of the aorta from aortic insufficiency; dilatation of the left ventricle.

gravity of the effusion is always less than that of the heart itself; therefore, with accumulating effusions, *i. e.*, as soon as the lateral portions of the pericardium are filled, the fluid will occupy the upper portion of the cavity, and the heart itself the lower. Even relatively slight effusions will increase the cardiac dulness in the dorsal decubitus, because the fluid is then collected against the anterior thoracic wall. If the patient be slightly raised from the recumbent posture, the fluid first collects at the superior bulging of the pericardium, in the neighborhood of the great vascular trunks, beneath the upper end of the sternum, and there pushes the lungs aside. Therefore, quite early in pericardial effusions the cardiac dulness reaches high up under the sternum or in its neighborhood, and assumes a characteristic triangular shape, with a blunt apex above and a broad base below. This triangular form is nothing more than the expression of the shape

of the portion of the dilated pericardium which lies against the anterior thoracic wall, and since the pericardium is wider at its diaphragmatic portion than at the great vessels, the lungs are pushed further aside at the lower than at the upper part. Pericardial distention shows especially plainly at the so-called cardiohepatic angle (Fig. 136), for the lung is very early pushed aside to the right of the sternum, and so changes this angle, normally about 90° or slightly more, to a much more obtuse angle.[1] An erect posture makes the dulness broader and somewhat lower than in the dorsal decubitus (if the effusion be larger), because the fluid, following gravity, flows further forward. Adhesions of the pericardium may prevent the application of any rules for determining the shape of the pericardial dulness.

Under normal conditions (see p. 240) a depression of the cardiac dulness occurs in the upright as compared with the recumbent posture; and the same depression of the upper borders of dulness during the sitting posture has been observed in actual enlargement of the heart from valvular lesions. Therefore we cannot always diagnose a pericardial effusion from the alteration in dulness noted above in the change of posture from lying to sitting. The action of gravity upon the enlarged heart may depress the diaphragm and so cause a lower position, or it may be that more venous blood is retained in the lower half of the body in the vertical position, so that the auricles are hot so completely filled. But if the erect posture produce a pronounced broadening of the lower part of the dulness, it is certainly more suggestive of a pericardial effusion than if it produce a mere depression of its upper border.

DISLOCATION OF THE HEART DULNESS IN TOTO

The position of the diaphragm varies with the age and the sex, and is responsible for variations in the situation of the heart which are permanent for the individual. Orthodiagraphic examinations (see p. 229) should be compared in this connection.

Otherwise the position of the movable organs of the thoracic and abdominal cavities at any given moment is the result of the muscular and elastic forces pushing or pulling them on every side and of the limitations to their mobility. The position of the heart is essentially due to the position of equilibrium in which the mediastinum is held between the two pleural cavities and to the position of the diaphragm. Any change of the diaphragmatic position or any disturbance of the equality of pressure between the two pleural cavities will produce a dislocation of the heart.

The pathologic dislocation of the heart contingent upon a dislocation of the diaphragm will be especially marked if the latter develop slowly, because a gradual stretching overcomes the resistance which makes a dislocation of that part of the diaphragm upon which the heart rests so difficult (fixation of the central tendon by the mediastinum, esophagus, aorta). *Meteorism, ascites,* and *voluminous abdominal tumors* push the heart *upward; emphysema* and *collections of fluid* or *air* in the pleural cavities push it *downward.*

A pathologic dislocation of the heart to the side ensues if the negative pressure in one pleural cavity become less markedly negative, or if it become positive. The heart will be pushed toward the side where the absolute pressure is less, *e. g.*, large collections of air or fluid in one pleural cavity dislocate the heart to the opposite side. Thoracentesis generally proves that an effusion which dislocates the heart to any

[1] [Rotch has emphasized the value of this sign in the diagnosis of pericardial effusions in children.—Ed.]

extent is under positive pressure; nevertheless, an effusion under negative pressure would exert a similar dislocating action, for such an action does not depend upon the absolute height of the pressure, but upon the difference between the pressures affecting the two sides of the mediastinum. The heart is merely pushed to one side until this difference in pressure is equalized. The practical importance of this fact, that even a fluid effusion under negative pressure may dislocate the heart, is the warning it gives us always to avoid the risk of introducing air into a chest by aspiration, whether the heart be dislocated or not.

Pathologic dislocation of the heart may occur not only when the negative pressure on one side becomes less negative or becomes positive, but also when upon one side of the mediastinum it becomes still more markedly negative. Here the action is more that of suction than of pressure, and is observed in pleural effusions which have led to a retraction of the lungs. As the exudate becomes absorbed, the heart is drawn over *toward the affected side* to fill the empty space. In fresh pleurisy the heart is pushed *toward the healthy side*. In retraction of the lung from other causes than pleurisy, *e. g.*, from interstitial pneumonia or tuberculosis, the heart is likewise dislocated to the affected side. It may remain there permanently from continued tugging, or it may gradually return to its normal position from a gradual distention of the lungs.

There is no law to determine how deformities of the thorax will dislocate the cardiac dulness.

The cardiac dulness in *situs inversus* and in *dextrocardia* occupies the right side, forming a sort of reflected image, symmetric to its normal form and position.

By starting from the normal relations we can easily understand the form and position of a dislocated cardiac dulness. Slight dislocations (from pleural effusions, etc.) produce only a lateral displacement, while marked dislocations occasion both a lateral and a pendulum movement. On account of the normal oblique position of the heart, such a pendulum movement probably occurs more readily in dislocations to the left; whereas, on account of the resistance of the central tendon of the diaphragm, a similar pendulum dislocation to the right requires much more force. The results of pathologic findings and the experiments of Ferber[1] finally settled the much disputed pendulum movement of the dislocated heart.

If the heart be dislocated by a pleural effusion, the dulness of the latter usually merges with the cardiac dulness so that only the borders of the other side of the heart are demonstrable by percussion. If the heart be dislocated to the left, its left edge will assume the same position as in left-sided cardiac dilatation. If retraction of the right lung or a left-sided accumulation of air or fluid crowd the heart considerably to the right, the right cardiac boundary and even the apex-beat (exactly as in dextrocardia) may be found in the neighborhood of the right mammillary line or even still further outside. Both superficial and deep cardiac dulness will be found to the right of the sternum; the former will merge into the liver dulness, and the latter will run around the superficial dulness, in the shape of a concentric border, from above and to the right. We can differentiate the result from *dextrocardia* either

[1] Die physikalischen Symptome der Pleuritis exsudativa, Habilitationsschrift, Marburg, Elwert, 1875.

by the signs of right pulmonary retraction, by the pleural dulness which occupies the place of the normal heart dulness, or by the signs of a left pneumothorax; from *situs inversus*, by the normal right-sided position of the liver.

Fig. 147 shows a large left-sided pleural exudate dislocating the cardiac dulness to the right; Fig. 149, a right-sided pyopneumothorax pushing the cardiac dulness to the left. From these figures it can be seen that in dislocation of the heart the lung edges may be so completely pushed aside as to make the entire cardiac dulness superficial, as in enlargements of the heart (see p. 242) and pericardial effusions. (See p. 248.)

If the heart be pushed upward by abdominal distention, the cardiac dulness not only lies higher, but also appears larger, *i. e.*, broader than normal. This is partly due to the retraction of the lung edges away from the heart in consequence of the limitation of space in the thorax. (See pp. 228, and 242.) The heart dulness may even be twisted by a sort of pendulum movement into a horizontal position, because the apex of the heart, which lies upon the movable portion of the diaphragm, is lifted up to the level of, or even higher than, the base.

TOPOGRAPHIC PERCUSSION OF THE LIVER

NORMAL LIVER DULNESS

Clinicians have often attempted to determine a superficial and a deep dulness for the liver just as for the heart, *i. e.*, to bound the anterior surface lying directly against the thoracic and abdominal wall, and to estimate the height to which the liver in the dome of the diaphragm rises into the thorax. The latter determination would be of very little value even if it were possible. The highest point of the liver lies far removed from the anterior thoracic wall; and in large persons with well-developed chests it is beyond the range of the percussion blow. Again, although we can obtain a relative dulness (a diminution of the fulness of the tone) above the lung-liver boundary corresponding to the wedge-shaped form of the lower edge of the lung, yet the upper limit of this dulness will almost always be lower than the highest point of the liver. But, as stated above, the estimation of the highest point of the liver is of little value. The liver is applied closely to the diaphragm, and so the upper liver boundary merely coincides with the position of the diaphragm, and we can determine that accurately enough by estimating the position of the upper border of the heart, the lung-liver boundary, and the liver edge. If the diaphragm be high, the lung-liver boundary and the liver edge are always high. If the diaphragm be low, the reverse is true. The lower liver boundary, which is generally easy to determine by percussion, usually shows whether the organ is increased or diminished in size. An enlargement of the liver pushes the lower liver edge correspondingly downward; except, though rarely, when the muscular resistance of the diaphragm is diminished, *e. g.*, with circumscribed tumors of the upper liver surface, *abscesses*, or *echinococcus cysts*. Even here the estimation of the so-called "relative liver dulness" is apt to be so unreliable as to be of little value, for the superficial lung-liver boundary is probably always somewhat elevated by such a growth.

Ordinarily, therefore, we are contented with estimating by percussion the part of the liver applied to the abdominal wall and situated beneath the edge of the lung. Under favorable circumstances we can map out a superficial dulness such as is pictured in Fig. 125. At the sharp edge of the liver this dulness is naturally so slight that only very light percussion appreciates the dulled note, while stronger percussion sets the underlying intestines in vibration. In the same way very light percussion is essential near the lung, as is naturally requisite in determining any superficial border, for otherwise the resonant tone of the adjoining lung tissue obscures the dulness and renders an exact definition impossible. Stronger percussion, however, brings out very clearly the superficial liver dulness higher up, corresponding to the thickness of the layer of the liver percussed. The upper borders of the superficial liver dulness coincide with the lower borders of pulmonary resonance. They can be plainly demonstrated from the front to the back. To the left of the median line, the superficial hepatic dulness merges with the superficial cardiac dulness at the fifth to the sixth rib between the left parasternal and mammillary lines (Fig. 136, p. 234). The possibility of distinguishing an inferior border of the superficial or deep cardiac dulness depends upon how far the left lobe of the liver reaches to the left. (See p. 234.) In the median line the inferior border of the superficial hepatic dulness lies halfway between the navel and the base of the xiphoid process, sometimes even higher. In the right mammillary line it reaches the edge of the ribs or projects slightly below them, and it lies upon the tenth rib at the right middle axillary line. All these measurements refer to patients who are breathing quietly and in the recumbent posture. The inferior edge of the liver behind cannot usually be plainly demonstrated on account of the thickness of the muscle layer.

The author protests against making statements about the absolute height of the liver dulness because no general value can as yet be attached to such measurements; but in concrete cases the vertical diameters of the liver dulness at the different arbitrary lines should be measured in order to recognize any changes in the liver size during the observation of the same case.

ACTIVE AND PASSIVE MOBILITY OF THE LIVER DULNESS

The liver dulness also possesses an active mobility with respiration, and a passive mobility with an alteration of the patient's position. The active and passive mobility of the upper edge of the superficial liver dulness coincides with the corresponding mobility of the pulmonary border (p. 225 et seq.). The active mobility of the lower liver border corresponds to the respiratory mobility of the dome of the diaphragm, and is much less than that of the pulmonary border. When a patient lies upon his left side, the passive mobility of the lower liver edge is shown by a depression of the right lobe. When he lies upon the right side, the reverse occurs (rotation of the liver about a sagittal axis). The liver is more difficult to percuss in the sitting or standing posture, on account of the increased tension of the abdominal walls. The lower liver border is occasionally elevated in these positions, probably because the increased intra-abdominal pressure pushes the liver to some extent upward, and thereby rotated about a frontal axis, it is turned up on edge. In this case the pulmonary hepatic boundaries are elevated somewhat in the erect posture. If the abdominal walls be lax, the weight of the liver produces the reverse effect. (See Lung-liver Boundary.)

PATHOLOGIC DISLOCATIONS AND GROSS CHANGES IN THE LIVER DULNESS

In "situs inversus" the liver lies in the left upper abdomen, symmetric with its normal position. Its dulness corresponds to the reversed position. Free air in the abdominal cavity nearly obliterates the liver dulness, because the air will be collected at the highest points. (See the Section upon Comparative Percussion of the Abdomen.)

Changes of the Upper Border of the Superficial Liver Dulness.—The upper border apparently lies higher than normal if a pathologic dulness from the thoracic organs (pleural effusion or lung consolidation) be superimposed upon the liver dulness. It is, therefore, necessary to resort to other methods of examination to determine whether it is a genuine high liver dulness or a normal liver dulness plus a pathologic pulmonary or pleural dulness (see below under Comparative Percussion). The existence of definite symptoms of a pleural effusion or a pulmonary consolidation will, of course, be of value.

The upper border will be higher if the liver be pushed upward in toto, *e. g.*, by increased abdominal tension. In this case the liver will ordinarily be rotated about a frontal axis, so that its inferior edge is elevated out of proportion to the lung-liver boundary, and the vertical breadth of the liver dulness appears abbreviated (angular position of the liver). If, at the same time, the liver be enlarged, despite its being canted upward, the lower edge may stand at its normal place or even lower.

Pulmonary retraction will also cause a higher position of the lung-liver boundaries.

A mere diffuse enlargement of the liver without marked increase of the intra-abdominal pressure, *i. e.*, without the liver being pushed upward, will not ordinarily cause an elevation of the lung-liver boundaries, because the organ will naturally enlarge in the direction of the least resistance (downward), and not against the diaphragm. With increased abdominal tension or if such an enlargement of the liver be excessive and occur so rapidly that its ligaments are not quickly enough stretched, a marked increase upward will result, *e. g.*, most frequently in unequal enlargements of the upper surface of the liver, which cause a localized pressure (tumors, echinococcus cysts, and abscess of the convexity). In most of these cases, however, the lower edge of the liver will also be pushed downward. Subphrenic abscesses produce practically identical percussion results with those obtained in tumors of the convexity.

Emphysema, either by crowding the diaphragm in toto downward or by filling the pleural sinus more completely with lung, will depress the upper border of the superficial liver dulness to a variable degree, depending upon which of these possibilities is present. *Pneumothorax* effects a similar result. Lessening of the intra-abdominal pressure, and exceptionally *enteroptosis*, will also depress the upper border of the superficial liver dulness.

Changes in the Lower Border of the Superficial Liver Dulness.—We have discussed some of these in the preceding section. They depend either upon a dislocation of the liver, a change in its size, or upon an association of these conditions. A careful attention to the entire clinical picture will differentiate these different conditions, *e. g.*, the etiologic and the accompanying relations (stasis); a palpatory appreciation of alterations in the consistence (cirrhosis, carcinoma); or

the absence of a dislocating cause. Conversely, the existence of a cause for dislocation (pleural effusion, abdominal distention, enteroptosis) suggests the possibility of dislocation; the existence of an enlargement or diminution in size, with careful attention to the other symptoms, suggests its improbability. All these are frequently such difficult problems in diagnosis that no constantly applicable rules can be given.

If the dislocating cause affect the entire upper or lower surface evenly, the lower edge of the liver will be pushed upward or downward as a whole, *i. e.*, symmetric and parallel to its former position (meteorism, ascites, emphysema). If, on the contrary, the pressure act unevenly, the organ will, by virtue of its attachments, be dislocated in an asymmetric fashion.

Accumulations of air or fluid in the right pleural cavity exceptionally rotate the liver about a sagittal axis. Conversely, a left pleuritic or left pericardial effusion will sometimes depress the left half of the liver. Similarly, though in a reversed way, a one-sided pulmonary retraction will elevate the liver.

Solid masses beneath the liver (packed intestines, tumors of the omentum, of the colon, of the stomach, and the like) may increase the liver dulness downward. Palpation or a carefully repeated examination generally discloses the true condition.

Conversely, intestines distended with air, overlying the liver and hiding part of it, may simulate a high position of the liver edge.

TOPOGRAPHIC PERCUSSION OF THE SPLEEN

NORMAL SPLENIC DULNESS; SEMILUNAR (TRAUBE'S) SPACE

The spleen lies in the left hypochondrium, between the ninth and the eleventh ribs (Figs. 121 and 122). Its long diameter ordinarily lies beneath the tenth rib. Its upper pole is situated only a few centimeters from the spinal column. Its lower pole reaches only to the middle or, at most, to the anterior axillary line. In relation to the course of the ribs, the long axis of the organ runs from behind and above forward and downward. The posterior upper third of the spleen lies hidden under the edge of the lung. The anterior and lower two-thirds ordinarily lie against the thoracic wall unless, as very frequently happens, intestines have been pushed in between the latter and the spleen.

Percussion can differentiate only that portion of the spleen which is uncovered by lung. Hence, it merely estimates a superficial dulness which can be accurately determined only by very light percussion. (See p. 211.)

To map out the free part of the spleen as perfectly as possible by means of percussion the patient should be sitting, standing, or lying upon the right side (the so-called lateral or oblique positions), because in the directly recumbent position the posterior portions of the spleen are not accessible to percussion. The lateral or oblique position has the advantage that the dulness due to ascites or to the contents of a well-filled stomach is shifted and so does not simulate the dulness of an enlarged spleen.

The normal splenic dulness in the sitting or standing posture is pictured in Fig. 126. The upper boundary of the dulness corresponds to that portion of the lung edge which intersects the eighth and ninth

ribs, and runs from the middle to the posterior axillary line. The anterior border of the dulness rarely reaches the anterior axillary line; in adults it is about 5 cm. above the costal margin. The dulness reaches as low as the eleventh rib. Measured in the long axis of the body, the height of the dulness varies between 5 and 6 cm. Posteriorly the splenic dulness merges into that of the lumbar region, due to the thick layers of muscles, not to the kidneys. (See p. 256 et seq.)

In changing from the sitting or standing to the recumbent posture, the splenic dulness is but slightly dislocated and then inconstantly either upward or downward as a whole. The cause of this displacement has been discussed upon p. 226 (passive mobility of the lung borders). (See p. 226.) The anterior boundary then usually remains the same. The splenic dulness is only slightly dislocated forward and downward in the oblique and lateral postures, because, although the left lung then assumes a deeper position, at the same time more of the upper part of the spleen is covered by the lung. A splenic dulness which projects beyond the anterior axillary line, even in the oblique and lateral posture, is abnormal.

The beginner should practise splenic percussion upon patients first in one position, then in another, in order to control his results.

It is impossible to map out the portion of the spleen lying above the edge of the lung, *i. e.*, to determine a deep splenic dulness. The spleen is a comparatively small organ, covered outside by the lung, and inside in contact with the stomach and intestines, so that a percussion stroke strong enough to penetrate the lung would set the tympanitic stomach into vibration. Besides, the differentiation of that part of the spleen covered by the lung has no practical value, because, just as in the case of the liver, any alterations can be easily recognized in the accessible part. (See p. 251.)

Percussion of the spleen is frequently not so simple as the above description would indicate. The spleen may be abnormally broad behind, or may lie abnormally high, so that it practically escapes percussion, though its size be within physiologic limits. With meteorism, especially when the distended intestines push the spleen upward and backward or crowd between the spleen and the thoracic wall, the vibration of such large air-containing cavities may make it almost impossible to differentiate so thin a solid organ as the spleen. Again, solid or fluid stomach or intestinal contents sometimes simulate a splenic dulness. The right lateral or oblique position will generally prevent confusion due to stomach-contents, and a later examination will show the true state of affairs in regard to the intestinal contents. Despite every care, however, repeated examinations, varying strengths of percussion, changes of patient's position, it must be acknowledged that palpation is very much more trustworthy than the percussion of this organ.

Between the splenic dulness and the left limit of the liver dulness there is normally a tympanitic area due to the stomach or intestines. This space is bounded above by the lung border, below by the free costal margin, and is called the semilunar or Traube's space. It is important in the diagnosis of left-sided pleuritic exudations (Figs. 125, 126, and 146). Percussion cannot always differentiate this space above from the lung; but then a boundary line can always be constructed corresponding to the edge of the right lung.

GROSS PATHOLOGIC CHANGES AND DISLOCATIONS OF THE SPLENIC DULNESS

Enlargement of the spleen is ordinarily evident by an increase in the splenic dulness forward and downward (Fig. 144). If the splenic dulness project forward beyond the anterior axillary line, or if its vertical extent in adults measure more than 7 cm., the spleen may be considered increased in size.

Diminution or even a complete disappearance of the splenic dulness happens frequently enough in perfectly healthy men with normal spleens. It would be impossible to distinguish such a condition from a pathologic diminution, and the latter is clinically unimportant.

Pathologic dislocations of the spleen are of slight clinical importance. They are usually difficult to demonstrate. Although pleural effusions, meteorism, and tumors may dislocate the spleen, percussion will rarely be of much help, because

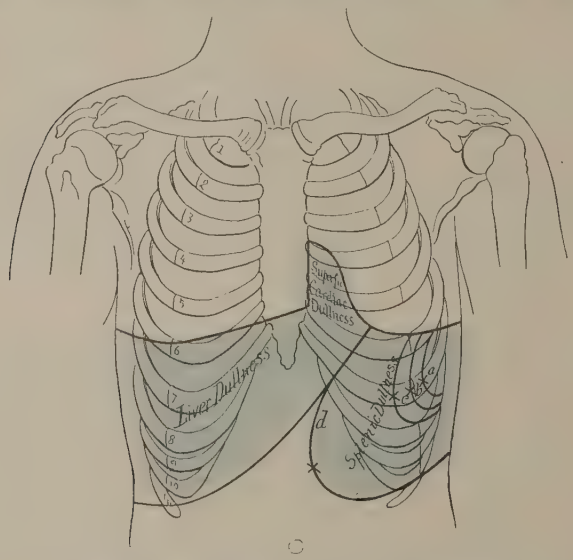


Fig. 144.—The splenic dulness in different grades of splenic enlargement (*a*, *b*, *c*, *d*).

either another dulness occupies that of the spleen, or else there is a resonant note (meteorism). Pronounced ascites pushes the spleen under the left lung so that it cannot be demonstrated.

With a marked dilatation of the stomach or enteroptosis the spleen is sometimes dragged downward and forward by the pull of ligamentum gastrolienale. It will then be more accessible than normally to percussion and palpation. (See later, Examination of the Stomach.)

Large pleural effusions occasioning a dulness in Traube's space, as well as enlargements of the liver, may cause the hepatic and splenic dulness to merge. (See Fig. 146.) Under these circumstances percussion may not detect even marked enlargements of the spleen.

TOPOGRAPHIC PERCUSSION OF THE KIDNEYS

The anatomic position of the kidneys (Figs. 121 and 122) precludes the possibility of mapping out their boundaries by percussion. Their deep

position prevents percussion from in front, and the thick layers of muscles behind cause a dulness which such a thin structure as a kidney could not increase. If we percuss a patient whose kidney has been removed, we can demonstrate the same vertical boundary of dulness as in a patient with an intact kidney. It corresponds to the outer edge of the sacrospinal muscles and has nothing to do with the kidney. Large renal tumors afford an intense dulness in the loins, projecting far beyond the boundaries of the sacrospinal muscles. If the tumor has pushed the other abdominal viscera aside and lies against the abdominal wall, it can be demonstrated from in front. Here it is of special diagnostic importance to demonstrate by percussion that the colon is anterior to the kidney (see below). Palpation is, however, far more important than percussion in this instance, as in the diagnosis of all other abdominal tumors.

TOPOGRAPHIC PERCUSSION OF HOLLOW ABDOMINAL VISCERA

(See also section upon Examination of the Stomach.)

Percussion is of no value for distinguishing one of these organs from the other, except under certain quite well-recognized conditions, viz., where the stomach or separate sections of the intestines are filled with air, fluid or solid contents. And then only superficial boundaries (*i. e.*, with light percussion) can be accurately estimated, because stronger percussion transmits the vibrations in all directions to an indeterminable and often to a considerable distance. Even superficial percussion is quite untrustworthy, because physiologically the position of the stomach and intestines varies considerably; because their superficial boundaries are rarely sharp; and because, although over different portions of the intestines the tympanitic tone varies in intensity and pitch, it is impossible to differentiate one region from the other. We can usually distinguish the swollen stomach or the distended colon from the small intestines by ordinary percussion. If this be not possible, the stick-pleximeter percussion or the auscultatory percussion (see p. 205) will differentiate them, provided there is enough increase in tension to produce a metallic resonance over the air-containing viscera. Both these methods of examination elicit at the edges of the organs either a sharp rise in the pitch of the metallic resonance or a sudden cessation of the resonance. However, every spot over a hollow organ does not necessarily give the same pitch of metallic resonance. Metallic resonance over an air-cavity may be present or lacking; and, again, its pitch may differ over different parts of the organ, especially if the latter be distended. If we trace the course of the colon distended with gas by means of the stick-pleximeter percussion, we can often appreciate entire scales of metallic resonance. Different pitches may be present even over the stomach. This is easily explained by the fact that a metallic resonance (see p. 207) is caused by the air in a hollow organ vibrating so as to give high, discordant overtones. In an irregularly shaped organ these overtones will naturally vary according to the spot percussed, and according to the direction of the blow. Hence, the value of this examination method must be limited, although we may make it easier by distending the stomach or colon with air. (See Palpation of the Abdomen and Examination of the Stomach.)

The demonstration by percussion of the tympanitic colon anterior to

a kidney tumor is very valuable for diagnosis (Fig. 167). The topography of this condition is described under Palpation of the Kidneys. It is safer to percuss both before and after distending the colon with [water and then with.—Ed.] air.

Inspection and palpation (especially after distending the stomach, see p. 424) generally furnish better evidence of the extent, position, and condition of the stomach and intestines than percussion. (See here special section, Examination of the Stomach.)

TOPOGRAPHIC PERCUSSION OF THE BLADDER AND OF THE UTERUS

The bladder when empty lies well hidden behind the symphysis pubis. When filled it ascends, even reaching, in cases of urinary retention, above the navel. As it rises it pushes the intestines aside and lies against the abdominal wall in the form of a vertically placed oval tumor, furnishing to light percussion an intense dulness, which corresponds pretty accurately to its extent and shape. If not very markedly distended and if some loops of intestines lie between it and the abdominal wall, part of the dulness may be deep (plainer to strong percussion), or there may even be no dulness present.

According to Müller's investigations, a bladder must contain between 500 and 600 c.c. before it will produce an appreciable dulness in normally developed women, and 360 to 500 c.c. in men.[1] If the rectum be distended, the bladder dulness projects somewhat more to the right. In lateral positions it is depressed to the deeper side, sinking at the same time somewhat into the depth of the pelvis, and so appearing smaller.

The condition of the bladder can be determined more accurately by palpation than by percussion unless the abdominal walls are very thick or rigid.

The pregnant or pathologically enlarged uterus acts like the bladder to percussion, and can be distinguished from it only by careful attention to other clinical conditions, by determination of the consistence, by means of palpation, by vaginal examination, and by catheterization.

COMPARATIVE PERCUSSION

Topographic percussion, as we have seen, furnishes us with conclusions as to borders, *i. e.*, as to the size and position of organs. Comparative percussion is concerned with the qualitative changes of the percussion-note over one and the same organ, and the conclusions to be drawn from such changes in regard to the condition of the organ and its surroundings. It is so designated because we compare the note over a certain spot of the body with the normal note over this spot, or with the note over adjacent or symmetrically placed (normal) areas of the same organ or of the same part of the body. It is a matter of choice whether we determine the relations of dulness of fluid effusions in the serous cavities by topographic or, as is done here, by comparative, percussion. The solid organs, however, belong exclusively to the domain of topographic percussion because it can only bound them (*i. e.*, determine their size, not their structure), and for this purpose topographic percussion is all that is essential. But with the air-containing organs of the abdomen, and more especially those of the thorax, the lungs,

[1] Berlin. klin. Woch., 1895, No. 13, p. 278.

we may determine countless qualitative modifications of the percussion-note which will furnish us most important information about pathologic changes at their surface or in their interior.

COMPARATIVE PERCUSSION OF THE THORAX

The ordinary note over the lung is resonant, loud, not tympanitic. The resonance or loudness varies with the thickness of the covering, and is also influenced by the adjacent organs (heart, liver, etc.). Beneath thick muscles or fat, *e. g.*, over the scapula and over the female breast, the percussion-note is less resonant than at other places. The intense dulness of the pulmonary tone in such spots can be modified only by very vigorous percussion. On the upper end of the sternum and the immediately adjacent areas the note is less resonant than over the sides of the thorax. This is due partly to the anterior mediastinum and its great vessels, and partly to the sternum supported by the unyielding framework of the upper ribs. (See p. 237.) Again, the pulmonary tone is less resonant (see p. 212 et seq., pp. 235, 250) over areas where the pulmonary tissue is thin, *e. g.*, the note over the apices or borders is normally duller than that over the intermediate, more voluminous portions of the lung. The examiner's ear gradually accustoms itself to these physiologic differences, so that they are instinctively appreciated. Marked convexity of the thoracic wall will cause a certain dulness, *e. g.*, in kyphosis and scoliosis. If we percuss upon a markedly convex spot of the thorax, a part of the percussion force is lost, because such a place yields so little; whereas a flat section of a rib oscillates to percussion in the direction of its greatest elasticity and so offers the best conditions for the transformation of the percussion stroke into vibrations. We must, therefore, be careful in drawing conclusions from the notes obtained over kyphoscoliotic chests, and physiologically as well, the resonance of the pulmonary tone varies decidedly according to the different configurations of the thorax.

Every structural change of the lung itself has an important influence upon the character of the pulmonary note, which may become abnormally resonant, tympanitic, or more or less dulled. The change can be appreciated by comparing the note with that over either symmetric or neighboring normal areas. Wherever the changes in the note include an entire lung, the beginner must compare the note with that of a healthy person. To the skilled these variations from the normal are easily appreciated without such comparison.

OCCURRENCE OF A DULLED NOTE WITHIN THE LUNG BOUNDARIES

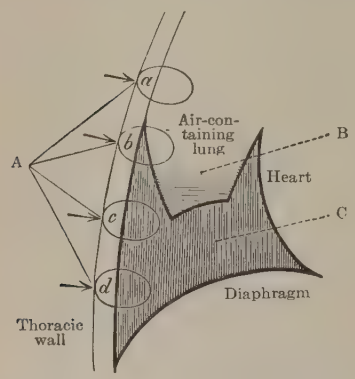
In order not to overlook slight dulness, it is always a good rule to utilize percussion of varying strengths. To make clear the importance of this precaution, it is necessary to enumerate the different anatomic possibilities which can produce a dulness in the lung tone.

Whenever the range of the percussion blow includes a smaller amount of air-containing lung tissue, or an area containing less air than normally, the tone will be dulled (p. 216 et seq.). This may be caused:

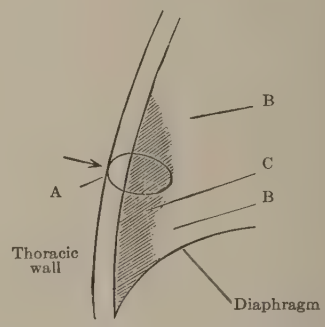
1. By the interposition of airless material between the lung and the thoracic wall: exudations, adhesions, tumors (Fig. 145, I).

2. By diminution or absence of air in the lung parenchyma itself,

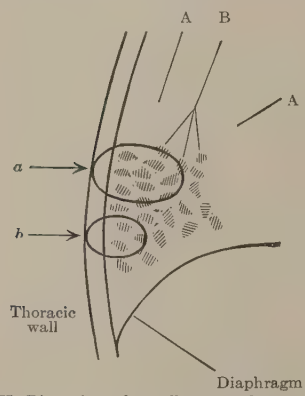
e. g., in (partial or complete) *atelectasis* (collapse of the alveoli), from compression or from closure of the bronchi with consequent resorption of the air; in *pneumonia*, from the (partial or complete) filling of the alveoli with an airless inflammatory exudate; in *new-growths*, from the tumor tissue taking (to a greater or less extent) the place of the lung



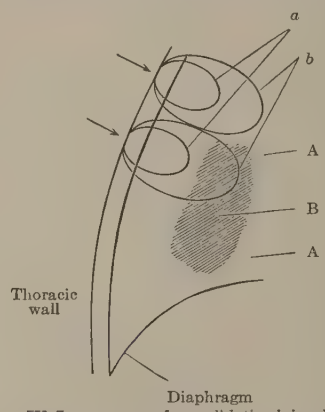
I. Pleural exudation: A, Sphere of action of light percussion; B, compressed lung; C, pleural exudate.



II. Superficial infiltration area: A, Sphere of action of light percussion; B, B, air-containing lung tissue; C, consolidated lung tissue.



III. Disseminated small areas of consolidation: *a*, Sphere of action of strong (deep), *b*, of light, percussion; A, A, air-containing lung tissue; B, small consolidated areas.



IV. Larger areas of consolidation lying deeper: *a*, Sphere of action of light, *b*, of strong (deep), percussion; A, A, air-containing lung tissue; B, consolidated lung tissue.

Fig. 145.—The different varieties (*i. e.*, methods of origin) of dulness of the lung tone. Diagrammatic frontal section through the thorax: I, Pleural exudate; II, III, IV, pulmonary consolidation.

tissue. These changes may occur in large areas which reach the surface of the lung (Fig. 145, II); in small scattered areas (lobular), partly at the surface, partly separated from it by lung tissue still containing air (Fig. 145, III); or, finally, in still larger areas situated in the depths of the lung (Fig. 145, IV). Each of these cases will furnish different percussion results.

If we percuss vigorously at *b* (Fig. 145, I), provided the exudate is not too thick, the lung can be so strongly vibrated that the dulness will be completely overlooked. To differentiate such a dulness as sharply as possible from the surroundings we should here percuss as lightly as possible. The same holds good for the condition represented in Fig. 94, II. The dulness is superficial in both instances, and can be best defined by regulating the range of the percussion blow so that the volume vibrated lie within the solid tissue, as in Fig. 145, II.

In Fig. 145, III, no very marked dulness can be evoked either by light (*b*) or by strong deep (*a*) percussion; both types will furnish only a slight dulness, because air-containing tissue will still be vibrated. The results of light or strong percussion will vary with the position, in relation to the surface, of the consolidation. If the consolidation as a whole be not very extensive, light percussion will bring out the dulness more plainly, because less air-containing tissue in the interior will be set in vibration.

Light percussion (range *a*) will demonstrate nothing with a larger, deeply placed area, as in Fig. 145, IV; but strong percussion (range *b*) will demonstrate a relative dulness.

Of course, we do not know beforehand whether there is any dulness, or if so, what kind of dulness; therefore it is always advisable to employ successively different strengths of percussion. Then we can decide as to the cause, relative position of the dulness (deep or superficial).

It is not to be expected that percussion can demonstrate every small area of consolidation. In fact, experience teaches us that isolated areas of consolidation, even though superficially located, to be appreciated must have a surface extent of at least a *few square centimeters*. If they lie more deeply, they must naturally be larger. But there are no generally applicable rules. For instance, multiple areas, if scattered thickly enough, need not be nearly so large as single areas to impair the resonance, *e. g.*, a lung richly studded with miliary tubercles will sometimes give a relatively dulled note. At other times, on the contrary, even thickly spread small areas will cause no dulness. The author has watched cases where the pulmonary resonance was absolutely normal during life, and yet at autopsy the lungs were everywhere infiltrated with sarcomatous nodules the size of nuts. There are many other important factors in this connection besides the amount of air contained in the lungs. For example, a relaxation of the lung tissue adjacent to solid areas will make the note more resonant than normal (see p. 271), and this hyperresonance may overbalance the dulness from disseminated tumor nodules or inflammatory consolidations.

In most cases other methods of examination must be resorted to in order to determine the cause of dulness. The most important characteristics of the different kinds of dulness of the lung tone will be mentioned in the following sections.

Pleuritic Dulness

Early in its formation a pleuritic effusion occasions a dulness in the lower posterior part of the thorax. This gradually rises higher, and pushes further forward, the boundary line running downward and forward (Figs. 146, 147, I, II). If the effusion increase still more, the

dulness extends forward, until finally the greater part of that side of the chest is dull, except that in the upper portions a slightly resonant note can be elicited. Exceptionally, the upper border of dulness may run circularly around the thorax instead of bowing down toward the front.

Why this line of dulness, which represents the actual position of the border of the exudate, is oblique has been a mooted question. The ordinary supposition is that the force of gravity determines the position of the exudate, and that the characteristic inclination is essentially produced by the patient's position during its development, and then fixed by encapsulation. If, then, a patient during the entire course of a slowly developing exudate be walking about, we should naturally suppose that the fluid would assume a horizontal level due to gravity. As in most cases, however, patients remain in bed with the head slightly raised, the line running downward and forward would correspond to a horizontal one for them. But this theory will not hold, for even if patients do walk about during the formation of an exudate, the same inclined line is almost always found. Some other cause must, therefore, be responsible for this peculiarity. The author considers that the following supposition is probably correct. Normally, the surface of the lungs is kept applied to the costal pleura by the difference between the air-pressure within the bronchi and the power of retraction or elasticity of the lungs. Now, it is physically impossible that the elasticity of so irregularly shaped an organ as the lung should be the same at all points of the surface. And wherever the retraction power of the lung is stronger, there it is that more of the intrabronchial air-pressure will be borne, because the physical force preventing the mechanic separation of the layers of the pleura is less. The posterior, more voluminous parts of the lungs undoubtedly possess the strongest retraction power, so that the exudate finds there the least resistance to its formation and accumulation. Thus, the boundary line bends downward and forward. In favor of this supposition is the fact that the exudate is not only higher, but also thicker behind.

As an argument against this hypothesis it has been stated that in hydrothorax the level of the fluid sometimes assumes a horizontal position, in the sitting and erect postures encircling the chest horizontally, while in the recumbent posture it disappears in front. The influence of gravity, however, in large dropsical accumulations must be very marked, so that the comparison is scarcely justifiable; but a very slight hydrothorax is, on the contrary, quite analogous to an exudate. The former exhibits the same line of dulness inclining downward from behind forward in the erect posture. (See p. 267.) With a freely movable fluid, not restricted by adhesions, one would naturally suppose that it would follow the law of gravity. Since it does not, there must be some power at work to fix its position, and the only conceivable power is that with which the air-pressure (evidently stronger in front and at the sides than behind) presses the lungs at the borders of the fluid against the chest. At first the exudate behaves in exactly the same way, and the reason it retains this original peculiarity after it has increased in size whereas the hydrothorax as it enlarges more and more follows the law of gravity, depends, in the former, upon the existence of adhesions at the edge of the exudate, which are very slowly absorbed and again pushed forward parallel to their line of formation. When the fluid of the latter (hydrothorax) attains a certain weight, and when the pressure under which it stands becomes positive, there is no longer sufficient resistance (in the absence of adhesions) to prevent free movability. Moreover, in medium-sized hydrothorax we can frequently prove that the change of level due to gravity follows but very slowly, which shows that the part of the lung in close proximity to the thorax still opposes a certain resistance to the dislocation of the fluid. The cases of pleurisy where the level of dulness runs a horizontal course are comparatively rare, and are by no means limited

to patients who walk about while the exudate is forming. In such cases some abnormal resistance behind, such as old adhesions or other pulmonary changes, probably oppose the accumulation of the exudate. All possible anomalies in the shape of the dulness may be explained by such assumption and by alterations in the elasticity of the lungs. It has been pointed out many times (Garland, Damoiseau, Ellis,[1] Heitler, and, more recently, Krönig and Hamburger) that the upper portion of pleural dulness is less intense near the spine than at some little distance from it. With a certain strength of percussion, therefore, it is possible to "bring out" an upper border of dulness, the highest point of which is at some distance from the spine. From this point the line drops both backward and forward. The author, however, does not consider this peculiarity usual nor does it conform most closely to the anatomic relations. This approximately triangular area of diminished dulness which, by this kind of percussion, can be mapped out along the spine from what the author considers the typical area of dulness, is known as "Garland's triangle." The author intentionally omitted mention of this phenomenon from his earlier edition and he believes too much stress has been laid upon it recently in the renewed and more active consideration of discoveries in physical diagnosis. In rare cases this paravertebral decrease of the dulness may be caused by an anomalous position of the exudate from adhesions; but otherwise the phenomenon under discussion belongs to the province of comparative percussion and not to topographic or border percussion, a distinction which is warmly defended in this book. As a few writers have properly emphasized, the phenomenon depends upon a stronger percussion than the author permits for determining superficial dulness. The upper part of the exudate is thinner, and so over it the dulness is less intense; hence, near the spine, vigorous percussion also evokes the resonant note of the healthy side. In fact, this is self-evident, and within any topographic percussion boundary different strengths of percussion certainly can bring out such qualitative variations in the note. They are, however, of no diagnostic value and may obscure the beginner's judgment of topographic relations. The renewed popularity of "Garland's triangle" makes this danger more imminent. As a matter of fact, "Garland's triangle" escapes demonstration if the percussion be correctly performed, *i. e.*, is sufficiently light, and the phenomenon is in reality the result of applying incorrect principles of percussion. Hamburger[2] objected that recent writers, including the author, had disregarded the surface as opposed to the deep action of the percussion stroke, concerned in this phenomenon; but the author believes that those who have properly understood the theoretic discussion of the principles of topographic percussion in this book will consider his criticism unfounded. In percussing borders, to obtain sharp localization and to prevent diffusion of vibrations—*in other words, to eliminate all possible surface action of the percussion blow*—percussion must be as light as possible, as has been repeatedly emphasized. The author does not disregard the surface action of percussion, but he considers it an undesirable side action, which confuses all conditions and is the essential cause of all errors in percussion and which should, therefore, be avoided as much as possible.

Besides the peculiarity of the boundary line, large pleuritic exudations are characterized by the marked intensity of the dulness (*flatness*). We seldom meet so intense a dulness in pulmonary consolidation,

[1] [*Ellis' Line.* In America the line of pleuritic dulness was first described by Calvin Ellis, at the March meeting, 1873, of the Boston Society for Medical Improvement (Boston Med. and Surg. Jour., January 1, 1873). He said: "When a pleural effusion is small, it may occupy a conical portion of the pleural cavity in the subaxillary region, where respiration and resonance may be wanting. But in a certain number of cases, when the effusion is quite large, if an accurate line be drawn, the flatness will be found to describe a curve, gradually approaching the spine toward the base of the chest, leaving a space from 1 to 3 inches broad between the spine and the line of flatness. In this space resonance will still be detected and respiration heard."

In a letter to the editors of the Boston Medical and Surgical Journal, January 23, 1874, Dr. George W. Garland reported a series of experiments on lungs of animals, in which he claims to have explained the curved line of dulness described by Ellis.

In a manual entitled Pneumo dynamics, by G. W. Garland, January, 1877, p. 6, the writer says that this line was first described by Damoiseau, of Paris, and redescribed by Ellis, of Boston. The latter was the first to trace its true shape. Ed.]

[2] Wien. klin. Woch., 1906, No. 14.

because in the latter the bronchi usually contain air and percussion still elicits a certain amount of resonance.

Of still more importance, however, in distinguishing pleural exudates from pneumonia is the demonstration of a *dislocation of the heart and liver* (see p. 249 et seq., and 253), and of a decided enlargement of the affected side of the thorax. (See p. 33 et seq.)

Corresponding to the position af the complementary pleural sinus (Figs. 120, 121, pp. 218 and 219 et seq.), the dulness in left-sided effusions reaches lower than the left pulmonary border. The position of the latter can be determined from the position of the lung-liver boundary. A dulness will then encroach upon the upper part of Traube's semilunar space (Figs. 125 and 126), between the spleen, lung, and liver. (See Figs. 146 and 147, I.) Such a dulness can be very easily demonstrated, and when present, is diagnostic of a left-sided pleural effusion; but accord-

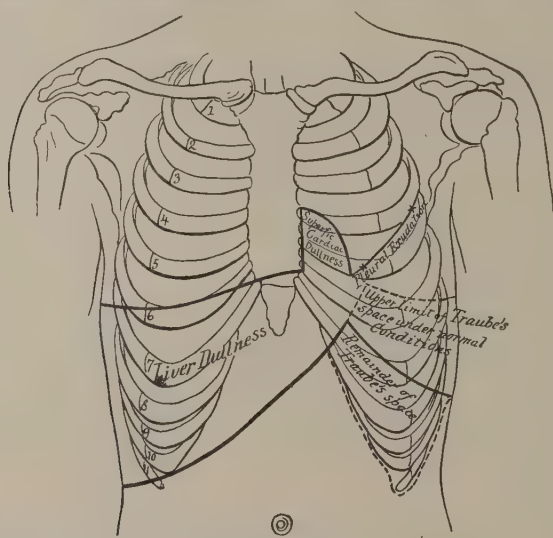


Fig. 146.—Dulness in left-sided pleural exudation. Diminution of Traube's space.

ing to the author's experience, left-sided exudates do not always produce this sign, because the complementary pleural sinus is often obliterated by early or previously formed firm adhesions, so that the exudate does not push into the sinus. Very large pleuritic effusions may force the diaphragm downward, so that the dulness which corresponds to the convex bowing of the diaphragm below may oftentimes project beyond the rib border as a narrow strip parallel to the costal margin (Fig. 147, I). This is rarely observed, because the intestines overlap the projection of the diaphragm.

Pleural effusions (unaccompanied by a pneumothorax, see p. 267) are rarely, if ever, freely movable with the change of the patient's position; this is conceivable only if there be no inflammatory adhesions at the borders of the exudate. Such exudates, more frequently serous than purulent, would furnish the same percussion results as a transudate (hydrothorax).

A pleural exudate limited by adhesions is more apt to be slightly movable. When the patient stands or sits up, the fluid shifts from behind forward inside the encapsulated space, presumably between the base of the lung and the diaphragm. Without any change in the boundary the intensity of the dulness thereby increases anteriorly and diminishes posteriorly. This peculiarity possesses some diagnostic importance and explains how it is possible to demonstrate plainly the existence of small exudates posteriorly only the moment a patient sits up, while later on it is much more difficult because part of the fluid flows more or less rapidly between the base of the lung and the diaphragm, resulting in a diminution both of the height and intensity of the dulness.

Light percussion is best suited to determine the boundaries of pleuritic exudates, since the dulness is superficial. Fig. 145, I, shows a frontal section of a pleuritic exudate. Above and below it is wedge-shaped, so that at the top and in Traube's space only a very light percussion could correctly determine the boundary.

If a pleuritic exudate become still larger, it compresses not only the part of the lung internal to the fluid (Fig. 145, I), but the entire lung, the pressure being exerted in the direction from the base of the lung to the apex; hence, the lung tissue above the exudate is under increased tension, and furnishes at first a hyperresonant and tympanitic note (p. 202), which soon, in consequence of diminished air content, becomes more and more dulled (p. 204). The note elicited over a pleural exudate can, therefore, at first be contrasted with the normal lung tone above it, later with a hyperresonant, tympanitic note, and finally with a relatively dulled note. In the last instance differentiation is often very difficult, but generally possible, because the note over compressed lung tissue whose bronchi still contain air sounds less intensely dulled than that over the exudate, and frequently possesses some tympanitic quality. Williams's tracheal tone (see p. 276) can sometimes be obtained when the pulmonary compression is very marked. (See Fig. 147 and the following pages for the percussion relations in large pleuritic effusions, and compare the pathologic dislocations of the cardiac and the liver dulness.)

Rauchfuss (Verh. der Gesellschaft für Kinderheilkunde, Breslau, 1904) has described a right-angled "paravertebral triangle of dulness" on the unaffected side in pleural exudate. The shorter side of the triangle is formed by the lower border of the lung from the vertebral column to a point 6 cm. or more to one side; the longer, by the vertebral column, up to the upper border of the exudate. Other authors (Baduel, Siciliano, Grocco) have also noted this phenomenon. In Italy it is known as Grocco's triangle. It may lead to a false diagnosis of effusion or of consolidation of the healthy lung. According to Rauchfuss, it is due partly to the dislocation of the mediastinum toward the unaffected side, so that the air content of the healthy lung is diminished near the vertebral column; partly to the transmission of too strong a percussion stroke along the surface (as in Garland's triangle, see p. 263) to the affected side. In the latter case it will disappear on the light percussion which the author insists upon for the determination of areas of superficial dulness. In the former cases it will persist. [The question of the clinical value of Grocco's triangle of paravertebral dulness has occasioned considerable difference of opinion in England and America; that of its mode of origin, still more. Ewart lays considerable stress upon a positive finding in the diagnosis of unilateral pleural effusion; believes that the triangle is rectilinear and not curved; acknowledges that a triangle of paravertebral dulness can also be produced by fluid accumulations in the abdomen, but states that its base is then broader than is the case in pleural effusions. In the latter neither the shape of the triangle nor its width

varies appreciably, but its highest point rises exactly to the level of the fluid itself. He considers that with a Samson pleximeter one can define the dulness more accurately than with the ordinary finger method. Ewart emphasizes the value of his so-called "Crucial Test and Counter Test" in discriminating between Grocco's triangle and one caused by some other condition. This check upon the finding consists of outlining the triangle first in the bowed, erect, or sitting posture, then in the lateral posture, the patient lying first upon the affected then upon the sound side. He claims that when the patient lies upon the affected side the triangle invariably diminishes; when upon the sound side, it persists, as in the erect posture, and is sometimes even increased in size. He has recently concluded that a Grocco triangle can be percussed out on both sides of the spine in bilateral pleural effusions as well as in ascites.

Thayer and Fabyan[1] have reviewed the subject exhaustively and have reported the existence of Grocco's sign in 30 out of 32 cases of pleural effusion. They regard the sign as practically constant in cases where there is free fluid in the pleural cavity or in which an encapsulated effusion impinges on the spine. They often found the respiratory murmur suppressed over the triangle of dulness and of a quality similar to that heard over the effusion. They confirmed Ewart's "crucial test."

Hollis[2] made a careful study of all the unilateral pleural effusions and pneumonias upon his service at St. Luke's Hospital and the New York Dispensary for three months. The triangle was present in about one-half of 18 cases of serous effusion, representing almost every variation in the amount of fluid. In one of them, with a very small amount of fluid, it was absent. Of 2 cases, with the chest full of fluid, it was absent in one and present in the other. As a rule, he found the highest point of the triangle lower than the level of the fluid. In 2 cases Ewart's "crucial test" failed. When, however, the patient was placed upon the sound side, the dulness was never intensified, but usually became less marked or disappeared. In 6 cases of pneumonia of one lower lobe he found the triangle twice, and once in a case of tuberculous consolidation with thickened pleura at one base. From these cases he concluded that the absence of the triangle is of no value in excluding the presence of fluid in the opposite chest, while its presence was no more than strong presumptive evidence of fluid in the opposite side. He explains the absence of the sign in so large a percentage of pleural effusions by the disposition of the fluid and of the adhesions.

All of these investigators are inclined to accept Baduel's and Siciliano's explanation—viz., that fluid in one side of the chest in contact with the spinal column will transmit a dull note to the opposite side through the medium of the spinous and transverse processes of the vertebræ and the heads of the ribs.

Although I have not considered this sign of sufficient value to keep careful notes on more than a dozen cases, my own experience coincides more nearly with Thayer's than with Hollis's. I have usually found the sign when I have looked for it, unless the fluid has been excessive or encapsulated in the lateral regions of the chest. A medium strength of percussion brings it out best, and if the finger be used as a pleximeter, the examiner must guard against touching the spine with it. "The triangle was first noted by Korányi in 1897 (in the fourth volume, p. 717, of Belgógyàszar Kezikönyze, and again in Eulenberg's Realencyklopädie der gesamten Heilkunde, xiii). It was independently rediscovered and more fully described by Grocco (Riv. crit. di clin. med., Firenzi, 1902)."[3]—Ed.]

If a pleuritic exudate become absorbed except for the fibrinous coating left behind, dulness may still persist. To distinguish such a condition from a fluid exudate necessitates a very careful attention to other symptoms and to other methods of examination.

As a rule, fibrinous thickenings produce intense dulness only when they are associated with signs of thoracic contraction. In such an event the atelectasis of the lungs usually adds its share to the dulness. We have no right to argue against a fluid effusion because the signs remain stationary, as exploratory puncture has frequently convinced the author of the presence of fluid in cases where the dulness which persisted long after the beginning of the pleurisy had been attributed to fibrin-

[1] Thayer and Fabyan, Amer. Jour. Med. Sci., January, 1907.
[2] Med. Record, January 13, 1906, p. 80.
[3] Quoted from Osler's Modern Medicine, vol. iii, p. 809.

ous thickening. Tapping such a chest usually causes a severe pain, because the compressed lung cannot expand; hence, interference is contra-indicated, and one should allow it to remain as a filled cavity. The author knows a patient with such an exudate who is undertaking high mountain climbing.

The height of the dulness will not always determine the amount of the exudate. If an exudate be well encapsulated, increase or decrease of the amount of the fluid is much more apt to produce an increase or decrease in thickness than in height, changing the intensity of the dulness rather than its extent. As mentioned above (see p. 262), abnormal relations of retraction or of elasticity are responsible for abnormal positions of exudates, *e. g.*, a marked collection beneath or to the median side of the lung. In such a case neither the intensity nor the extent of the dulness affords a clue to the real condition, but only a careful study of the other appearances, such as dyspnea, dislocation of the organs, enlargement of the affected side of the thorax, etc. These are all very important in localizing the point for tapping a pleuritic effusion.

Ferber has plainly demonstrated a dulness after injecting 120 cc. of fluid into the cadaver of a twelve-year-old child, and after 400 cc. into an adult. But in the living, as shown in the results of tapping, much smaller quantities of fluid are often demonstrable by light percussion.

Dulness of Hydrothorax

In general dropsy the dulness due to the transudation of serum in the thoracic cavity corresponds to that of a pleural exudate. Here, too, with small transudates, the boundary line tends to curve downward and forward. (See p. 263.) But as soon as the fluid has reached a certain amount it becomes more or less movable, and the upper border of dulness then assumes a horizontal level in every position of the body, although at first it may change its position but slowly (p. 263). A change from the horizontal to the sitting or standing posture elevates the anterior boundary of the resonant pulmonary tone. This is an important point in making a differential diagnosis between hydrothorax and pleurisy. Hydrothorax is, for the most part, bilateral, but frequently more marked upon one than upon the other side. If patients have maintained a constrained position upon one side, the hydrothorax is ordinarily more decidedly developed on the lower side, or even limited to that side. Hydrothorax does not often produce any dislocation, because it is commonly bilateral, and because there is ordinarily an accumulation of fluid in the abdomen at the same time. Traube's space is affected the same as by a left-sided exudate except, of course, that the dulness is movable.

Increased abdominal contents, pushing up the diaphragm and the lung boundaries, often obscure the diagnosis of a coincident hydrothorax. If the patient be raised from the horizontal to the sitting posture, the anterior borders of the lungs will be pushed upward, but this is of very little help, for the sitting posture compresses the abdomen, and therefore also elevates the diaphragm. Hence, we must examine either in the standing or lateral posture. In the former, a dulness appears in front and below, although, to be sure, a slight hydrothorax may be hidden in the erect posture on account of the depression of the diaphragm (pp. 222 and 225). A comparatively large hydrothorax in the horizontal lateral posture would furnish a strip of dulness running along the vertebral column, which could easily be determined by comparing the two sides. (See Fig. 148.)

Dulness of a Pleural Exudate when Combined with a Pneumothorax

If a pneumothorax has persisted for some time, a fluid inflammatory pleural effusion commonly results, which may be either purulent or serous (sero- or pyopneumothorax). The fluid then collects beneath the air in the deepest portions of the pleural cavity, and furnishes a dull

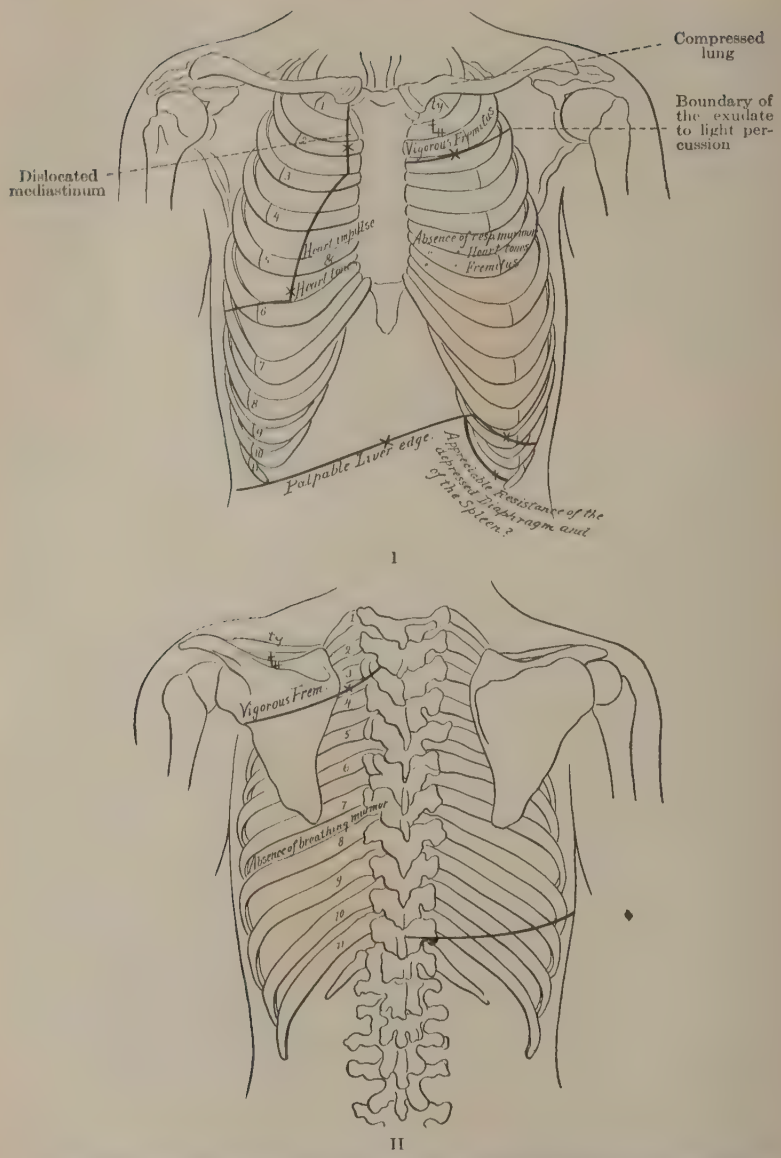


Fig. 147. Results of examination in a large left-sided pleural exudate. Pronounced dislocation of the heart, of the mediastinum, of the left lobe of the liver, and of the diaphragm. (See p. 416 et seq. for explanation of signs.)

percussion-note. Change of the patient's position produces the most decided mobility of this dulness, and such mobility is very characteris-

tic of this affection. In this condition pressure in the pleural cavity is, as a rule, strongly positive, and unless tied down by adhesions, the entire lung is separated from the thoracic wall by the air, so that the fluid can perfectly well follow the laws of gravity. The level of dulness is therefore exactly horizontal in every position of the patient. As there is no opposition, any change of posture produces an instantaneous change of the dulness (a contrast to hydrothorax). The fluid is not collected in the form of a wedge extending up between the lung and the chest-wall, as in ordinary pleurisy; but all of it is situated below the lung (Fig. 145, I). The consequence of this is that a considerable amount must be present before it becomes evident to percussion. In the beginning the exudate is sometimes completely hidden at the bottom of the thorax; and the high pressure of the pneumothorax depresses the diaphragm upon the affected side and makes it bulge downward. Not infrequently

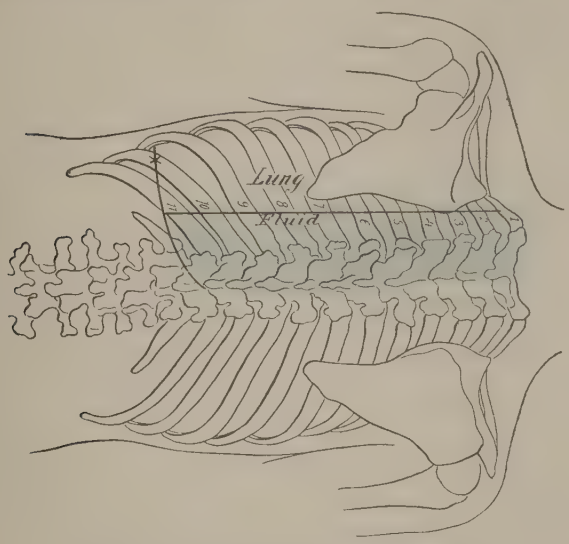


Fig. 148.—Dulness of hydrothorax in right lateral posture.

we can demonstrate the fluid by means of the succussion murmur (see p. 301) before percussion shows anything. As it increases in size a narrow band of dulness can be made out at the base of the lung, front and back. We are apt to obtain better results from percussion if the patient bend forward; or if he lie upon the well side and we percuss above the spinal column, in the same way as in hydrothorax (Fig. 148). Figs. 149 and 193 show the results of examination in sero- and pyo-pneumothorax.

If the lung of the affected side be more or less adherent at the onset of the pneumothorax, all the signs will be atypical. Even a very small exudate may then be appreciated by percussion. Although the relations of position are atypical, we should still expect a change of position in the dulness of the fluid.

Dulness of Hemothorax

If blood collect in the pleural cavity from traumatism, from the rupture of an aneurysm, or as the result of a hemorrhagic diathesis, the resulting dulness will ordinarily correspond to that of hydrothorax. Since the blood coagulates very slowly (after the lapse of days), this dulness will usually shift with change of the patient's posture unless some inflammation ensues, when coagulation and encapsulation will very soon fix it.

Dulness Due to Consolidation of the Lung (Inflammation; Tuberculosis; Infarction)

A consolidation af the lungs presents a less intense dulness than a pleural effusion, because the bronchi ordinarily remain full of air, and so aid in producing a partially resonant tone. The dull area is generally of different shape. It is less sharply bounded, because the consolidation gradually merges into healthy lung tissue. In the neighborhood of consolidations we frequently obtain a tympanitic or hyperresonant note, so that the dulness due to a consolidation is often so-called dull tympany. (See p. 271 et seq.)

In *croupous pneumonia* the dulness is more apt to be located behind and below. (See Fig. 194.) Frequently enough it corresponds to one or more of the lobes of the lung; it may, however, overlap these borders in an irregular way. (See Figs. 120, 121, and 122.)

In *bronchopneumonic consolidations* the dulness is situated either behind and below (see Fig. 196) or at the sharp anterior and lateral lung edges, or else in a narrow strip along both sides of the spine.

In *tuberculous consolidations* the dulness is most frequently localized at the apices (see Fig. 195) and at the sharp pulmonary edges, especially at the "lingula" which bounds the superficial cardiac dulness on the left. Miliary tuberculosis generally causes no dulness, but rather a hyperresonant tone (p. 272, 3). Very thickly studded miliary tubercles may, however, produce a diffuse dulness simulating a catarrhal pneumonia or chronic tuberculosis (p. 261).

Pulmonary infarctions, if large enough to cause physical signs, commonly occasion a dulness over the lower posterior portions of the lung, which at first is diffuse and not very intense, but which gradually becomes more marked and more sharply defined. (See Fig. 196.)

Dulness from Tumors of the Lungs, of the Pleura, and of the Mediastinum, from Substernal Goiter, and from Fatty Deposits in the Mediastinum

There is little characteristic about the dulness of tumors of the lungs and pleura, and this corresponds to their atypical topography. They furnish a marked dulness only when they have reached a considerable size, and then it is apt to be more intense than the dulness of inflammatory consolidations, because in the tumor tissue there are no hollow bronchi. The intrathoracic tumors springing from the mediastinum, as well as substernal goiters, furnish a somewhat characteristic dulness over the upper end of the sternum; it projects from there laterally into the territory of the lung, where it is generally more or less distinctly separated from the cardiac dulness and has the shape of an hour-glass. If these tumors involve the pleura, they are frequently accompanied by pleuritic exudates, with the corresponding physical signs. Here may also be mentioned the dulness, described by von Hampeln, which is caused by fatty deposits in the mediastinum. This may sometimes lead to the erroneous diagnosis of a dilated heart.

Dulness of Pulmonary Cavities

Tuberculous and bronchiectatic cavities of the lung furnish a dull note if the cavity be filled with secretion instead of with air. It is quite characteristic for such a dulness to be replaced by a resonant, often a tympanitic, note after copious expectoration. But usually the dulness does not disappear completely because it is due in part to the thickening of the pulmonary tissue in the neighborhood.

Dulness from Pulmonary Edema

It is ordinarily assumed that pulmonary edema gives rise to a hyperresonant note (see the following page), yet a series of autopsies has convinced the author that if a pulmonary edema be of long duration, the air in the area infiltrated with fluid becomes absorbed or rises in bubbles into the bronchi, so that a very intense dulness may result, especially in the postero-inferior portions of the lung. This dulness can be differentiated from the dulness of consolidation by its rapid alteration and by the absence of bronchial breathing, because the bronchi, too, are mostly filled with fluid. Here it is really a sort of fluid or serous infiltration of the pulmonary parenchyma.

Dulness of Atelectasis of the Lungs

This is in general like the dulness of consolidation. *Obstruction atelectasis, i. e.,* one due to a catarrh and plugging of the bronchus, with subsequent resorption of air from the alveoli, ordinarily furnishes a dulness like that of small areas of consolidation (see above). Later on the atelectasis is commonly transformed into a consolidation. *Compression atelectasis,* from dislocation or enlargement of the heart or from the crowding of the diaphragm upward and the consequent compression of the sharp pulmonary edge, also furnishes a dull tone. This occurs upon a larger scale from fluid accumulations in the pleura, where the part of the lung covered by the fluid, and later that lying above the fluid, is robbed of its air content. (See p. 265.) Marked cardiac enlargement compresses the lung and often causes a very extensive dulness of the left posterior and inferior portions of the lung. It is frequently wrongly diagnosed as a pleural effusion or pulmonary consolidation. Some pleural exudates exhibit the paravertebral triangle of dulness upon the sound side as a result of partial atelectasis. (See p. 265.)

During the formation of all kinds of atelectasis the tissue is relaxed, so that the normal tone is first transformed into a hyperresonant or tympanitic note, and finally, on account of the diminution of the air content, into a dulled note. (See p. 203.)

Dulness of Pulmonary Retraction

By pulmonary retraction is understood that chronic change of the lung which results from indurative (shrinking) consolidation and atelectasis. The result of percussion in the retraction associated with pulmonary tuberculosis corresponds essentially to that in tuberculous consolidations. The retraction resulting from a pleurisy causes either a localized dulness corresponding in shape and extent to the antecedent exudate, or if the whole lung be compressed, a diffuse relative dulness of an entire lung. Thick pleuritic adhesions or exudates which remain stationary frequently increase the intensity of the dulness.

Dulness from Diffuse Dilatation or Diverticulum of the Esophagus

(See later, Examination of the Esophagus.)

ABNORMALLY RESONANT (HYPERRESONANT) AND TYMPANITIC NOTES WITHIN THE PULMONARY BORDERS

We have already described upon p. 204 et seq. the conditions which may give rise to a hyperresonant or to a tympanitic note over an area characterized normally by a non-tympanitic one.

Hyperresonant or tympanitic notes within the pulmonary borders occur as follows:

1. In *pulmonary emphysema* diffused over the entire lung. The very typical percussion-note of emphysematous lungs is called a "box-note" ["boardlike."—Ed.]. The name is sufficiently descriptive. Some authors describe it merely as an abnormally resonant pulmonary tone; others as a low tympanitic note.

2. In *relaxation of the pulmonary tissue* from retraction due to a diminution of space in the thorax. This occurs in dislocation upward of the diaphragm, in intrathoracic and intrapulmonary tumors, in consolidation, in pleural effusions, in cardiac enlargements, and in peri-

cardial effusions. When the diaphragm is pushed upward, the note may be uniformly abnormally resonant over both lungs. If the relaxation of the pulmonary tissue be localized, as in the other cases mentioned above, the abnormally resonant note will be chiefly noticeable adjoining the cause of the decrease in space. Thus, just above the pleuritic dulness the retracted lung gives an abnormally resonant or tympanitic note. In all these conditions the more marked the relaxation of the lung, the more nearly tympanitic this abnormally resonant pulmonary tone becomes. If the space be still further decreased, so that the lung is compressed, the note becomes dull.

3. In *relaxation of the pulmonary tissues from structural changes.* To this type belong diffuse pulmonary edema and the localized inflam-

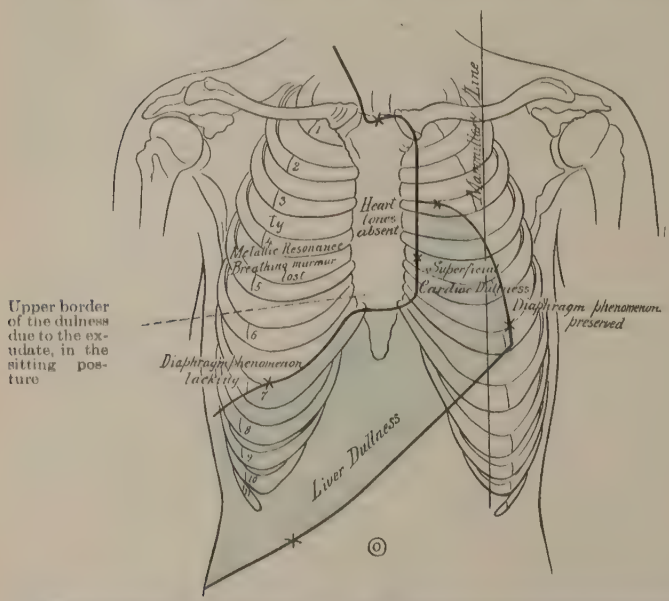


Fig. 149. Results of percussion in a right pneumothorax—dorsal decubitus (the exudate is, therefore, not demonstrable in front): resonance overlapping the territory of the lung; dislocation of the liver, heart, and mediastinum; superficial cardiac dulness restricted at the right.

matory edema which adjoins a consolidation, both as a precursor and as a residuum of the inflammatory consolidation. With the onset of the edema the normal pulmonary tone becomes first abnormally resonant, next hyperresonant, and finally tympanitic. Pronounced edematous saturation of the lung may ultimately produce a dulness. (See p. 271.) The relaxation of the pulmonary tissue in beginning obstruction atelectasis, due to the plugging of a bronchus by secretion or by a foreign body, also belongs to this category. Another transition occurs here, as well from the hyperresonant to the tympanitic note, and finally, if the atelectasis become complete or lead to consolidation, to dulness.

4. In *pneumothorax* (Fig. 149). In most cases the percussion-note

becomes abnormally resonant, but only rarely tympanitic. The most frequent type is the so-called valve pneumothorax, in which the air is under such marked pressure that the note is usually non-tympanitic (p. 204). It is, however, generally tympanitic in open pneumothorax, where the air is under the atmospheric pressure only (postoperative empyema). The chief distinction between the normal lung tone and the note of a pneumothorax is that the latter projects noticeably beyond the normal lung boundaries, because the complementary pleural sinus is filled with air. In right pneumothorax the liver dulness is diminished from above, the cardiac dulness from the right. (See p. 241 and Fig. 149.) In left-sided pneumothorax the splenic dulness disappears and the cardiac dulness is either diminished or, more commonly, disappears (p. 241). Very frequently distinct dislocation can be observed. Sometimes, though not constantly, the resonant note over a pneumothorax presents a metallic character, which usually can only be appreciated with the stick-pleximeter method of percussion. (See p. 205.) Again, it may exhibit all sorts of variations in the pitch. (See following pages.) If the pneumothorax be combined with an inflammatory fluid effusion, and this is the rule when it has persisted for any length of time, the fluid shifts completely with change of the patient's position, and very much more rapidly than in hydrothorax. In every position of the patient we find, then, that the lower part of the thorax is dull; and that above the dulness, separated from it by an exactly horizontal line, is the resonant note of the pneumothorax (p. 269 and Fig. 149).

5. In *cavities of the lungs* (tuberculous, bronchiectatic, and abscess cavities). As a rule, the cavities are at least partly filled with secretion and they are surrounded by tuberculous or consolidated inflammatory tissue, so that percussion over them ordinarily elicits a dull note. (See p. 270.) Stronger (deep) percussion, or the expectoration of the secretion, transforms the dull into a tympanitic note. A very large cavity containing a great deal of air, or one located very superficially and surrounded only by a thin layer of consolidated pulmonary tissue, will furnish an abnormally resonant note, and even with light percussion, a tympanitic one. Smaller cavities (up to the size of several cubic centimeters), and even very large cavities, when situated deeply, generally escape demonstration by percussion. The stick-pleximeter percussion method will sometimes, though not often, demonstrate metallic resonance and change of pitch over cavities. (See pp. 205 and 275 et seq.)

6. Diaphragmatic hernias in the region of the lung, containing intestines, will cause a loud tympanitic note. They can be distinguished, especially, from pneumothorax, by their irregular shape and by the intestinal borborygmus, mostly of metallic character.

7. See p. 888, under Examination of the Esophagus, in regard to the tympanitic note of esophageal diverticula.

SPECIAL PERCUSSION PHENOMENA OVER THE THORAX

Metallic Resonance Over the Thorax

See p. 207 in regard to the origin and peculiarity of metallic resonance.

Metallic resonance is most frequently observed in *pneumothorax*. (See the preceding page.) It is favored by the size of the air space and by the smoothness of the walls, and is most readily demonstrated by the

stick-pleximeter method of percussion, combined with auscultation. Metallic resonance, is, however, not a constant sign of pneumothorax, because it requires a peculiarity in the shape of the air space and a certain degree of tension of the inclosed air. If the air exist under too slight or even under too high a pressure, the metallic resonance disappears. It often requires a certain strength of percussion to make it audible, and not infrequently it can only be appreciated at certain places. In most cases the metallic note is too weak to be appreciated at a distance, *i. e.*, without coincident auscultation.

The metallic resonance of a pneumothorax frequently disappears during aspiration; or, in case it was not present beforehand, aspiration may bring it out. This is due to the influence of the tension of the inclosed air.

The metallic resonance of a pneumothorax frequently exhibits distinct variations in pitch, depending upon whether we percuss the patient in the sitting or recumbent posture. This is plainly due to the mobility of the fluid in the pleural cavity, with change of the patient's posture. A deepening of the note in the sitting and an elevation in the recumbent posture (Biermer's change of tone) is more frequently noted than the reverse. The height of the metallic resonance varies inversely with the longest diameter of the air space (see p. 205); therefore we assume that in the former case the diaphragm, under the weight of the exudation in the sitting posture, drops downward. If the note become higher in sitting up (the reverse), we assume that it is due to the resulting diminution of the air space by the rise of the exudation in the sitting posture. The pitch of the metallic resonance varies in different places; hence, in such an examination we should always percuss the same spot.

In pneumopericardium an abnormally resonant tympanitic or non-tympanitic note takes the place of the cardiac dulness, sometimes accompanied by a dulness from the exudate and sometimes not. (See p. 242.) A blended metallic resonance similar to that of pneumothorax can at times be demonstrated. The patient's posture may also influence the intensity and the pitch of this metallic resonance (change of tension of the air, dislocation of the heart and of the exudate).

Pulmonary cavities only rarely furnish metallic resonance, because they do not often fulfil the conditions for its establishment. (See p. 205.) They are either too small, have too irregular or too thick walls, *i. e.*, are situated too deeply. The last-named factor may prevent the occurrence of metallic resonance because it opposes an interrupted vibration of the air-space. (See p. 205.) If a metallic resonance be obtained over a pulmonary cavity, similar alterations in pitch may be brought out, concerning which see pp. 208 and 275 et seq.

Diaphragmatic hernias within the thorax may also give rise to a metallic resonance (see below).

CRACKED-POT RESONANCE (CHINK OF COINS) OVER THE THORAX

Cracked-pot sound (see pp. 205 and 208 as to its origin) may be produced while percussing a normal thorax under entirely physiologic conditions, *e. g.*, over the lungs of a crying child, or, provided the thorax is yielding, over an adult's lungs while he is talking, or over some people's lungs during forced expiration with half-open vocal cords. Vigorous

percussion, proximity to the trachea, and open mouth all favor the production of this resonance. The sound under physiologic circumstances is assumed to rise at the narrowed glottis, because the percussion blow causes the sudden escape of air. (See pp. 205 and 208.)

It can also be noted over relaxed or partially consolidated pulmonary tissue under all those conditions which furnish abnormally resonant or tympanitic pulmonary tones, *e. g.*, at the borders of pleuritic exudates and in the neighborhood of consolidations. Its explanation under these circumstances is not yet entirely clear, *i. e.*, whether here, too, it is due to a stenotic murmur (pp. 205 and 208) arising, as in the crying child, at the glottis, or as seems more likely, in the latter case, *in loco*. The percussion blow may produce a momentary compression of bronchi, as well as a coincident escape of air through them. However this may be, the author's experience has convinced him that if the conditions which give rise to the noise, even in healthy persons, be absent, *i. e.*, speaking, straining while the glottis is half open, etc., cracked-pot resonance rarely results from the above-mentioned pathologic conditions (relaxation, consolidation). Cracked-pot sound has a certain significance in the diagnosis of pulmonary cavities. It is very common, especially with rather strong percussion, over small superficial cavities (a few centimeters in diameter) which, as is usual, communicate with a bronchus. It is probably due here to the production of a stenotic murmur at the opening of the bronchus into the cavity. Marked emaciation will favor the production of the sound. If the above-mentioned conditions which are apt to favor its production under normal circumstances be absent, the author attributes considerable importance to this phenomenon in the diagnosis of pulmonary cavities.

CHANGE IN THE PITCH OF THE PERCUSSION-NOTE OVER THE THORAX

Wintrich's Change of Tone and Williams' Tracheal Tone.—If the patient open his mouth during percussion, the pitch of a tympanitic pulmonary note, or of a metallic resonance over pulmonary cavities, will be raised, while if the mouth be closed, the pitch will be deepened. This is *Wintrich's phenomenon*. The patient should breathe naturally, and the note over the two sides of the chest must, of course, be compared during the same phase of respiration, because change in the latter causes variation in the pitch. (See p. 276, Friedreich's Phenomenon.) It is a sign of a cavity, and arises if the cavity communicate with the bronchus and transmit the resonance into the trachea, and from there into the mouth. The pitch in the mouth must vary as it is being opened or shut, according to the laws of open and closed pipes. If we approach the ear to the patient's mouth, we can readily be convinced that the change of pitch in reality depends upon an admixture of the percussion tone with the individual tone of the mouth. Hence, Wintrich's change of tone is not absolutely pathognomonic of a cavity. As a matter of fact, we do observe this same sort of tone change in percussing over the supra- and infraclavicular fossæ from consolidation or contraction of the upper part of the lung or from marked compression by pleuritic exudate, because vigorous percussion will readily transmit the vibration through the thickened tissue to the main bronchus and to the trachea. The note which sounds dull to light percussion then becomes tympanitic, and opening and shutting the mouth will

evoke the same Wintrich tone change. The name *Williams' tracheal tone* has been given to this phenomenon when due to such consolidated or contracted areas of lung without cavities. If Wintrich's change of tone appear and disappear, depending upon the body posture, we speak of it as the *interrupted Wintrich tone change*, as contrasted with the *simple Wintrich tone change*. Secretion closes the communication between the cavity and the bronchus, and so the sound is not transmitted. This peculiarity will sometimes aid in differentiating the Wintrich phenomena from the Williams' tracheal tone.

Gerhardt's Tone Change (Gerhardt's Phenomenon).—If the pitch of a tympanitic note or of the metallic resonance over a pulmonary cavity change with the patient's position, we speak of this change as Gerhardt's phenomenon. Fig. 150 (*a* and *b*) explains this.

A cavity contains both air and fluid. The fluid is freely movable. The diameter of the part of the cavity containing air is longer in the recumbent than in the erect posture, or vice versâ. If the lung axis of the cavity lie transversely, the note in the recumbent should be compared with that in the lateral posture. Hence, percussion will produce a note of deeper or higher pitch according to the patient's position. This would naturally lead us to believe that Gerhardt's phenomenon

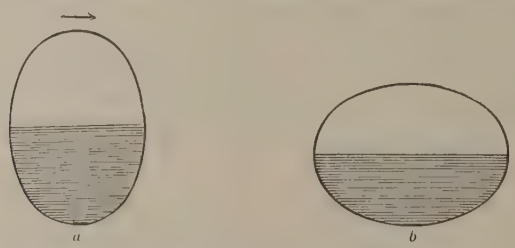


Fig. 150.—Gerhardt's phenomenon.

not only demonstrates the presence of a cavity, but also the direction of its longer axis; in other words, tells us about its shape. From a practical standpoint, however, we should remember that a distinct Gerhardt's phenomenon is rare; that other methods of examination, such as auscultation, are quite as diagnostic; and besides that slight differences of percussion-notes with change of position may be, within physiologic limits, due simply to alteration in the tension of the thoracic wall without any cavity within the chest. As simple a condition as is represented in Fig. 150 is rarely observed upon the autopsy table. The cavities are more irregularly shaped, so that there is more than one long axis to influence the pitch; and, besides, the variation of the tension with change of position plays a very important part, because the walls of many cavities adhere to the costal pleura.

Wherever Gerhardt's tone change could be demonstrated exactly as is explained above, the secretion flowing forward in the sitting posture should furnish a dulness at the lower border of the tympany and so clinch the diagnosis.

Friedreich's Phenomenon, or the Respiratory Tone Change.—Inspiration raises the pitch of the tympanitic or metallic note over a cavity and expiration deepens it. This is Friedreich's phenomenon. However respiration slightly alters the pitch of the note over a per-

fectly normal lung, so that this phenomenon is not diagnostic of cavities unless it be very marked and perceived at a circumscribed and otherwise suggestive spot. The phenomenon depends upon the variable tension of the lungs in the normal case, and of the cavity-wall in the pathologic case.

Biermer's Phenomenon.—The pitch of the metallic resonance over a sero- and pyopneumothorax is deepened in the erect and raised in the recumbent posture. (See p. 205.) Biermer's change of tone is in a way identical with Gerhardt's, except that the former author limited his description to the metallic resonance over pneumothorax, and Gerhardt, to the tympanitic note over pulmonary cavities.

DEMONSTRATION BY PERCUSSION OF A DIMINISHED RESPIRATORY ACTION IN PARTIAL CONSOLIDATIONS OF THE LUNGS

For the demonstration of such partial pulmonary consolidations as cause neither obvious dulling of the percussion-note nor characteristic findings on auscultation, it is often of great interest to determine whether, over the spot in question, the same change in tone between inspiration and expiration may be noted as over neighboring or corresponding areas. Normally, especially if percussion be not too light, the note is more resonant during inspiration, on account of the increased volume of air. The determination of the absence of this physiologic difference may be sufficient to establish the diagnosis of partial consolidation. This test is especially useful in the demonstration of incipient tuberculosis at the apex. Comparison should, of course, always be made with the corresponding spot in the other lung.

COMPARATIVE PERCUSSION OF THE ABDOMEN

A. The percussion-note over the abdomen becomes *more resonant:*

1. From distention of the intestines with gas (*meteorism*). The tension of the intestinal coils is increased and so dulls the note, but the increased volume of gas seems to overbalance the dulness; therefore, the note becomes sometimes higher, sometimes deeper, according as the influence of the increase of volume or the increase of tension predominates. The increase of volume tends to deepen the pitch; the increase of tension, to raise it. The more the tension increases, the less tympanitic the note, until eventually it will resemble a hyperresonant lung tone.

2. From an accumulation of air within the peritoneal cavity, pneumoperitoneum (perforation of stomach or intestine). Here the influence of the volume of air and of the tension acts precisely as in meteorism. If the air accumulation be freely movable, it naturally occupies the highest point of the peritoneal cavity and overlaps the liver, sometimes enough to obliterate the liver dulness. If, as commonly happens, an exudate be associated with the accumulation of air in the peritoneal cavity, the inferior portions become dull. This dulness shifts exactly as in pyopneumothorax, and so always presents a horizontal level. The stick-pleximeter method of percussion ordinarily brings out or emphasizes the metallic resonance over an air accumulation in the abdominal cavity.

B. The abdominal note becomes *dulled:*

1. In a diffuse way, from diminution of the gaseous contents of the intestines (starvation, scaphoid belly of meningitis tuberculosa).

2. In a circumscribed way, from solid or fluid material filling the intestinal coils. (In regard to a possible confusion between abundant fluid in the intestine and free fluid in the peritoneal cavity, see section 6.)

3. From tumors which are situated in the intestines, which lie between the intestines and the abdominal walls, or which, arising from below, push the intestines aside. Palpation bounds these much more accurately, so that the only value of percussion is to determine whether the intestine or stomach lies in front of the tumor or not, by the presence or absence of a superficial dulness over the palpable resistance. For this purpose it goes without saying that we must employ as light a percussion as possible, in order to avoid vibrating neighboring or deeper-lying intestinal coils. It is difficult to determine deep dulness over the abdomen, so that percussion has very little value in localizing deep-lying tumors. (See p. 257.)

4. From a large number of empty and contracted intestinal coils.[1] These may produce quite an intense localized dulness.

5. From inflammatory infiltrations of the intestinal walls or of the peritoneum. Palpation also appreciates them as resistances resembling tumors. To this group belong the dulness noted in the right iliac fossa in perityphlitis and that of chronic inflammatory and tuberculous adhesions. The dulness can sometimes be sharply defined, sometimes not. Light percussion is necessary because dulness, if appreciable, is superficial. Palpation again generally furnishes more accurate data of the topographic relations.

6. From fluid effusions between the intestines and the abdominal wall. At a moderately acute stage inflammatory effusions are frequently encapsulated by adhesions, and then furnish a circumscribed, irregularly shaped dulness. Inflammatory serous effusions which are slow in their development, *e. g.*, tuberculous peritonitis, and even acute purulent effusions, are not necessarily encapsulated. We shall obtain from them a more or less intense dulness in the dependent portions of the abdomen, shifting with the patient's movement and presenting an approximately horizontal level in every position. This horizontal level of dulness may, however, frequently be interrupted at one or two places, where separate intestinal loops are adherent or where marked tympanites may press them against the abdominal wall. This change in the position of the dulness need not appear instantly in every case, even though adhesions be absent, because the distended intestines are likely to oppose some obstacle to the movement. *Ascites* or *dropsical effusions in the abdomen* (general dropsy, portal stasis) furnish similar percussion results. The dulness is always superficial, so that percussion must be light in order to bound the fluid dulness.

A free fluid effusion in the abdomen must attain considerable dimensions before it produces distinct dulness. F. Müller[2] found, in experimenting upon the cadaver, that in children one year old 100 cc. could not be demonstrated; that 150 cc. gave a relative dulness; and that 200 cc. gave an absolute dulness, shifting with change of position. In adults, 1000 cc. furnished no distinct dulness; but with 1500 cc. a dulness was perceptible in the dependent portions (lumbar regions); while with 2000 cc. the dulness reached a hand's breadth and became absolute. He rightly emphasized the greater accuracy of percussion of the living body; and this is in accordance with countless clinical and pathologico-anatomic experiences. The more favorable results in percussing the living depend, the writer believes, on the

[1] F. Müller, Berlin. klin. Woch., 1895, No. 13, p. 278.
[2] *Loc. cit.*

one hand, upon the greater elasticity of the living abdominal walls, which, therefore, furnish a better localization of the percussion blow; and, on the other hand, upon the fact that during life the movements of the intestines prevent the loss of any fluid between separate coils of intestines.

Very large fluid effusions furnish a dull note over the greater part of the abdomen. But even then a rounded tympanitic area persists very characteristically at the highest point of the abdomen, *i. e.*, the epigastrium, corresponding to the top of the intestinal coils floating in the fluid. Free fluid effusion in the abdominal cavity can thus be differentiated from the equally marked abdominal distention due to cystic tumors. In women such cysts frequently originate in the ovaries; in men, very rarely in the pancreas. With these cysts the dulness is most marked in the middle of the abdomen, because they quickly grow toward the middle line, the direction of least resistance, and crowd the intestines backward.

(See paragraph 7 in regard to the demonstration of free fluid effusions in the abdomen, with coincident edema of the abdominal walls.)

There may occur an abdominal dulness which resembles that caused by ascites in that it changes with the position of the patient and preserves a horizontal level, but which is due to fluid in the intestine, not in the peritoneum. Such a condition is known as *pseudoascites*. The differential diagnosis between it and true ascites is generally not very difficult. Pseudo-ascites is usually characterized by the presence of diarrhea and of succussion, by the less definitely circular boundary of the dulness, and by the slower change in the position of the dulness when the patient is moved. The general clinical picture of ascites is also, of course, lacking.

7. From thickening of the abdominal walls, whether on account of fat-accumulation or of edema. The edema is ordinarily localized in the dependent portions, so that percussion may confuse it with ascites. Palpation of the abdominal walls, and the fact that the dulness does not shift with a change of the patient's position, will generally prevent a mistake. If the edema be combined with ascites, the movable fluid can sometimes be demonstrated only in the knee-chest position, because the edematous lateral walls of the abdomen furnish so much dulness.

AUSCULTATION

AUSCULTATION IN GENERAL; INSTRUMENTS

Auscultation in its broadest sense means the examination of the body by the sense of hearing. It should include the appreciation of any sounds the body may furnish, whether heard near by, at a distance, or with the aid of instruments, *e. g.*, the cough, the voice. In the narrow and more usual sense, auscultation includes only the diagnostic method of listening to the body by means of some specially constructed sound-conducting apparatus or by means of the ear directly applied.

A few experiments and essays antedated the practical listening to the interior of the body.[1] Auscultation was, however, first practically employed by Laënnec. His work upon auscultation was published in the year 1819. In it he not only instituted these methods of examination, but ventured definite conclusions which were based upon several years' study. He also invented the stethoscope. Many scholars have since then developed the scope of auscultation; among them notably Skoda,

[1] Hippocrates recognized the succussion noises, named for him, as well as the pleural rub, which he compared to the creaking of leather.

Wintrich, Zamminer, Traube, Bamberger, A. Geigel, Th. Weber, and Gerhardt.

In regard to method, we distinguish between an *immediate* or *direct* and a *mediate* or *indirect auscultation*. In the former the examiner's ear is applied directly to the patient's body; in the latter he listens with the aid of an instrument called the stethoscope.

According to the author's opinion, the essential quality of a good stethoscope is not, as was contended by Laënnec, and since his time by many others, its capability of intensifying the tone vibrations. Unless an examiner is hard of hearing, stethoscopes which transmit to the ear vibrations intensified by resonance are by no means the best, because they are bound to alter the tone to some degree. Examples of this type are the instruments of Voltolini, Hüter, and König. In that of Hüter, the opening of the sound funnel is closed by a simple rubber membrane; in that of König, by two rubber membranes with an air-space between, whose form can be changed by blowing upon it into a lens-shaped resonating chamber. The microphone, devised to intensify the sounds, has not thus far proved practical.[1] The requisite, then, for a good stethoscope is not so much the capacity to magnify as the capacity to transmit the tones to the ear, at least not markedly weakened. This essential is fulfilled by practically all the countless stethoscopes met with in practice, in the use of which we are sure that we hear only what is appreciated by the ear. The stethoscope might therefore be considered superfluous and only immediate auscultation practised. But it has certain advantages, the most important of which is that it enables us to auscultate an exactly circumscribed spot to the exclusion of the neighborhood; in other words, to exclude the sounds of adjacent body parts. In cardiac diagnosis this is absolutely necessary. On the other hand, immediate auscultation offers certain disadvantages in the direction of convenience and cleanliness; besides, in the supraclavicular it is impossible, in the infraclavicular region very difficult, to apply the ear directly. In some cases, however, especially in listening at the back, immediate auscultation is of advantage. Direct contact can then, of course, be avoided by interposing a soft towel between the patient's body and the examiner's ear. Faint bronchial breathing occurring at the beginning of pulmonary consolidation in pneumonia can often be detected only by placing the ear directly against the thorax. This is particularly true in the case of young children.

Stethoscopes have been made in the most varied forms and out of the most varied materials. They ordinarily consist of a hollow stem of wood, hard rubber, or metal, with an enlarged, slightly funnel-shaped tip at one end, and an ear plate, with a hole in the middle, fastened perpendicularly to the other end of the stem. The funnel-shaped end is placed against the skin of the patient, and the ear of the examiner is applied to the ear plate as closely as possible. The ear plate is in some

[1] The so-called *phonendoscope*, recently so extensively advertised and discussed, is in reality nothing more than the old resonance stethoscope, which long ago fell into disuse on account of the alteration of the tone. Its popularity is probably due to the name and to the appearance of the instrument. Like the microphone, its principle of construction is based upon the false assumption that the main trouble in auscultation consists in the difficulty of appreciating the sounds. Any one who has had much experience will complain rather of an embarrassment of riches in auscultation. The real difficulty lies in judging the significance of the sounds, and this difficulty will not be made any less by using an instrument which magnifies unimportant or artificial accessory noises.

[Despite the author's objections to the resonating stethoscope, its use in America is so universal that I believe a word in its support might be in place here. The choice of a stethoscope is, after all, quite a matter of custom and convenience. Many good stethoscopes are made in America, especially the Tiemann and Ford models, the favorites in New York City, and the Gannett model, so often selected by clinicians in Boston and Baltimore. The resonance is decided with any of these instruments, but I have not found that it seriously detracts from their practicability. The Bowles' model, a type of phonendoscope, is warmly recommended by many of the younger clinicians. In my opinion it has many advantages, although I still depend upon the other models for most purposes. One especial advantage is that it can often be used when another type of instrument fails, *e. g.*, when a patient is recumbent and too sick to be moved. Then, by slipping it under the patient's back, one can often obtain an approximately accurate idea of the breathing over the bases of the lungs behind.—Ed.]

instruments concave, in others convex. For most observers the former shape seems to adapt itself better to the ear. To carry the instrument conveniently in the pocket, it is desirable to be able to separate the ear plate from the tube by unscrewing or in some other way. There is no advantage in substituting for the ear plate an olive-shaped peg adapted to fit into the external canal of the ear. Experiments have shown that the canal which is bored through the tube in the axis of the stethoscope should have about the same diameter as the entrance of the external ear.[1] In order not to cause the patient pain, the edge of the funnel end must be well rounded. The width of the funnel varies with different instruments. A wide funnel has the advantage of receiving sound waves over a large area, and therefore, in general, of transmitting the sounds more powerfully to the ear. On the other hand, a narrow funnel has the advantage of better isolating the sounds and of modifying them less by resonance. It is of some advantage, therefore, to possess a stethoscope with a wide funnel at one end and a narrow one at the other, in either of which the ear plate can be inserted by means of a conical peg. The funnel should not be too long. The long bell-shaped funnel ends of many hard-rubber stethoscopes really confuse the respiratory murmurs, and often in a very marked way, by resonance. The length of the cylindric part of the instrument is of minor importance.

Flexible stethoscopes transmit the sound from a funnel through a tube or tubes to the ear of the observer. This is the principle of most of the above-mentioned resonance stethoscopes. They are very convenient, especially the binaural, and a furnish a very loud tone; but the resonance is confusing, and the slightest movement in handling gives rise to perplexing murmurs. The same difficulty occurs even in the binaural stethoscope (devised recently by Camman and warmly recommended by Pel) and in similar instruments in which accompanying noises are hindered by making the sound-conducting tube partly quite firm, partly of very dense tubing. After many attempts with all these instruments, the author must recommend for practice the ordinary single-barrel stethoscope, for he is convinced that in a method of examination which is already difficult itself, it is not advisable to complicate the affair for the sake of external convenience and to use instruments which possess such essential faults. He believes that the use of flexible stethoscopes very often leads to gross diagnostic errors. They are absolutely necessary only for auscultating one's own body.

The Technic of Auscultation.—The stethoscope should be applied very carefully, so that the edge of the funnel makes an air-tight connection with the skin; the ear should be lightly applied to the ear plate without leaning the head upon it. Tilting the stethoscope should be avoided, because it is very painful for the patient and prevents correct auscultation. The best way is to hold the stem with the thumb and forefinger lightly applied near the funnel end, so that the slightest movement can be readily felt and corrected. In direct auscultation the ear should be placed in close contact with the body. It is often well to close the other ear with the finger.

AUSCULTATION OF THE RESPIRATORY ORGANS

The immediate, as well as the mediate, method should be used in auscultating the lungs, for some sounds, such as faint bronchial breathing (see p. 288), are better appreciated by applying the ear directly to the chest, and an exact localization is of less value than in cardiac diagnosis.

It is exactly in these cases (in general rare), where the tones are so weak as to be indistinguishable, that the tone-increasing or resonating stethoscope is useless, for its modification of the sounds increases the difficulty. It may so destroy the sharp distinction between vesicular and bronchial breathing that gross errors result. The sources of error which may arise from involuntarily moving the stethoscope while auscultating the lungs will be mentioned later.

It is advisable to auscultate during normal, and then during exaggerated, respiration, and over any suggestive places both during and after cough, as well as to listen in such places to the loud and the whispered voice.

[1] A form of stethoscope, long abandoned as impracticable, but recently revived, has a solid instead of a hollow stem. This, however, does not convey the sound properly and should be discarded.

THE NORMAL VESICULAR RESPIRATORY MURMUR

A characteristic sighing or sipping noise, perhaps resembling a very soft "f," is heard over a healthy lung throughout inspiration; during expiration there is either no sound, or at the beginning a very short, faint noise. The latter is rather difficult to describe; it is apt to be lower pitched than the murmur during inspiration, and is slightly rustling, or over certain places slightly blowing, in character. Its duration corresponds normally to less than a fifth of that of the inspiratory murmur. These two sounds constitute the normal breathing murmur—the so-called vesicular breathing. Its presence shows us that the lung parenchyma at the spot of auscultation not only contains air, but also breathes—that is, during inspiration air enters the alveoli. The inspiratory murmur is evidently the essential characteristic of vesicular breathing.

Numerous theories have been suggested in explanation of this vesicular breathing, but as yet there is no one definitely accepted. Laënnec, the inventor of auscultation, assumed that vesicular breathing was caused by the rubbing of the inspiratory air stream against the walls of the fine bronchi or infundibula. But if friction exist, it must act, not between the walls and the air, but between the outer layer of air, which rests nearly motionless against the walls, and the more central actively moving current. Laënnec's theory, however, did not lay any emphasis upon the friction taking place at the outer boundary of the air stream, *i. e.*, between the air and the walls of the bronchi and infundibuli, and might be stated to-day by saying vesicular breathing is the acoustic expression of the friction caused by the entry of air into the pulmonary parenchyma. It has also been objected that the current of air entering the bronchi during inspiration is not rapid enough to cause friction noises.

Baas has advanced a more recent theory, which many authors believe disproves Laënnec's. Vesicular breathing he regards as a modification of the blowing noise which arises in the larynx and trachea during respiration, which is transmitted through the bronchi to the interior of the lungs, and thence through the air-containing lung to the observer's ear, and which acquires, because of the interposed air-containing tissue of the lung, its sipping vesicular quality. The following experiment was made in proof: An inflated lung was placed upon the larynx of a living man, the laryngotracheal murmur was auscultated through this lung, and it was expected that the blowing murmur would be transformed into a sipping vesicular breathing by the air-containing lung. The author has never heard anything but a weakened blowing tracheal murmur in performing this experiment. It is, in fact, difficult to imagine how the tracheal murmur, with an expiratory portion the equal of or stronger than the inspiratory portion, could be both qualitatively and quantitatively modified by the interposition of an air-containing lung. Nor does clinical evidence support Baas' theory, for, as soon as a bronchus is plugged by secretion or by a foreign body, no vesicular breathing can be heard over the pulmonary area supplied by that bronchus until the bronchus becomes free again. This surely proves that inspiratory filling of the lung with air is necessary to produce vesicular breathing. The pathologic modifications of vesicular breathing similarly disprove the Baas theory, *e. g.*, we hear an intensified vesicular

breathing over circumscribed areas of lung when, for some reason, the breathing is more vigorous (compensatory); and, on the contrary, a localized diminished breathing wherever, for any reason, the corresponding lung area is limited in its movement (through lack of room or adhesions). Again, despite the increase of the laryngeal breathing noise in laryngeal stenosis, diminished vesicular breathing is heard over the lung. Further, the thicker the layer of lung, the more intense is the vesicular breathing, although, according to this theory, it should be diminished. Finally, systolic vesicular breathing, a respiratory murmur synchronous with the cardiac systole and not in the least dependent upon a laryngotracheal breathing murmur, speaks with certainty against the Baas theory, and decidedly favors the idea that vesicular breathing depends upon the pulmonary excursion. The author considers these arguments sufficient to discountenance Baas' theory.

Now, after all this critical discussion, what is the real explanation of vesicular breathing? In the author's study of the origin of vesicular breathing he demonstrated upon a man with congenital fissure of the sternum[1] that vesicular breathing arises from inflation of the lung tissue, even with the exclusion of every laryngotracheal murmur. This man had a hernia of the lung in the region of the sternal fissure which protruded externally to a marked degree when the patient strained, *i. e.*, increased his intra-abdominal tension. When this pulmonary hernia was auscultated at the same time that the patient strained, the most distinct vesicular breathing was heard, which was due to an expiratory filling of the pulmonary alveoli, and, since the laryngotracheal murmur was excluded by the closure of the glottis, we obtained a certain proof that the murmur of vesicular breathing is due to the local inspiratory movements of the pulmonary parenchyma. The author has recently had an opportunity to make a similar examination of the pulmonary apices of an emphysematous subject, which became inflated like balloons when the patient strained (Valsalva's experiment), and over which could be heard distinct vesicular breathing. In these examinations he could not determine whether the vesicular murmur was produced by the distention of the pulmonary tissue or by the friction in the interior of the inspiratory air stream in the smallest bronchi and alveoli. That is a fine point of no great significance. Stretching of the lung tissue may cause the murmur. The distention of separate lung alveoli doubtless does not happen at the same instant, and may produce a series of vibrations lasting over the entire inspiratory period, which together may cause the vesicular murmur.

To explain the normal brief expiratory murmur we must assume either that the weak remnant of the laryngotracheal breathing murmur is transmitted from the bronchi, or else that the expiratory murmur arises, like the vesicular inspiration, locally, through movements and rubbing in the lung during expiration. If the expiratory murmur have a plain blowing character, like that of the laryngotracheal murmur, the former hypothesis may be entertained. It should then be classed under the so-called physiologic bronchial breathing. (See p. 284 et seq.) If this blowing character be lacking, the expiratory murmur probably comes from within the lung, especially because the expiratory, like the inspiratory, murmur may be modified by local lung changes. The prolonged expiration in catarrh (see p. 287 et seq.) can be explained only

[1] Correspondenzb. f. Schweizer Aerzte, 1892.

by assuming such a localized origin. The elastic retraction of the lung in the beginning of expiration must be strongest and quickest; hence, the expiratory murmur is normally to be heard only at the very beginning of expiration.

Systolic vesicular breathing (mentioned above) is occasionally to be found both in healthy and in diseased individuals. Its origin is unknown, it has no pathologic significance, is heard only in the neighborhood of the heart, in slightly marked instances merely as a systolic accentuation of regular vesicular breathing. It certainly depends upon variations of the intrathoracic negative pressure (especially in the cardiac region) connected with the systolic diminution in the size of the heart (microcardia). Many so called accidental heart murmurs (see later) are nothing more than systolic vesicular breathing. Interrupted or cog-wheel breathing (see p. 287), if heard only in the neighborhood of the heart and if the interruptions be synchronous with the pulse, may, under some circumstances, depend upon the systolic accentuation of vesicular breathing.

PHYSIOLOGIC BRONCHIAL (MIXED) BREATHING MURMUR

Over certain areas of the normal lungs the respiratory murmur sounds bronchial. Such a murmur corresponds in most essentials to the laryngotracheal breathing heard over the larynx (p. 282). In contrast to the vesicular, bronchial breathing presents a blowing character and approaches to a definite pitch. We can reproduce the sound quite perfectly by vigorously inspiring and expiring with the mouth fixed as if about to pronounce the syllable "ha." We can simulate different pitches by changing the position of the mouth. In physiologic bronchial breathing expiration lasts longer and is more strongly accentuated than inspiration, exactly the reverse of the relation between them in vesicular breathing. The rima glottidis is narrowed during expiration, and that is a sufficient cause for an expiratory stenotic murmur or for an accentuation, as well as for its prolonged duration. Physiologic bronchial breathing is nothing more than the laryngotracheal murmur which originates at the upper air passages and is transmitted through the bronchi to certain areas over the lungs. Its intensity varies considerably in accordance with the individual peculiarities of acoustic transmission. In many men the laryngotracheal murmur is audible only over the neck, while all over the lung pure vesicular breathing can be heard, in others it is audible as physiologic bronchial breathing over more or less of the lung. Physiologic bronchial breathing is most frequently audible anteriorly over the superior portions of the lungs, and posteriorly in the interscapular space. This is due to the location of the trachea and great bronchi. The right bronchus is wider and a more direct continuation of the trachea than the left; hence this breathing is naturally more evident upon the right side and sometimes also over the upper part of the sternum. Vesicular breathing is almost always to be heard at the same time with the physiologic bronchial breathing; but if the respiration be especially faint, then the physiologic bronchial breathing will alone be heard, *e. g.*, a thick thoracic wall renders the appreciation of the vesicular breathing difficult. A so called *mixed breathing* is, however, the general rule, *i. e.*, during inspiration the vesicular, and during expiration the bronchial, character predominates. *Forced breathing, dyspnea, thinness of the thorax, any changes in the larynx and trachea which favor the production of a strong stenotic murmur* (compression of the trachea from the side by a goiter[1] and the like)

[1] In such a case the expression "physiologic bronchial breathing" signifies merely that the phenomenon does not depend upon any pathologic changes in the lung.

—all these will intensify physiologic bronchial breathing. A suggestion of physiologic bronchial breathing may very rarely be heard all over the lung, but more frequently along the spine and over most of the sternum.

Physiologic bronchial breathing may depend in some persons upon certain peculiar positions of the mouth. It may be considerably influenced, intensified, diminished, or even caused to disappear by altering the position of the mouth.

ALTERATIONS OF VESICULAR BREATHING UNDER PHYSIOLOGIC AND PATHOLOGIC CONDITIONS

INCREASED (PUERILE) AND WEAKENED VESICULAR BREATHING

The intensity of the vesicular breathing varies with the depth of the respiration and with the spot auscultated. It is weaker at the apices and borders, where the layer of pulmonary tissue is thin, than over the thick parts of the lung. Thick thoracic walls also weaken it. Children present an exceptionally loud and strong vesicular, so-called *puerile* breathing, with which physiologic bronchial breathing is often especially plainly mixed. Beginners are apt to mistake it for a pathologic phenomenon.

Pathologically, increased vesicular breathing is best designated as *sharp* or *increased vesicular breathing*. The author emphasizes these two adjectives because the expressions *sharp* or *increased* vesicular breathing and *rough* vesicular breathing (in regard to the latter, see p. 287), though fundamentally different from the acoustic standpoint, are often used synonymously. If ordinary vesicular breathing be represented by the sound of a soft *f*, increased vesicular breathing roughly corresponds to the consonants *ff*. The physiologic increased breathing (see preceding paragraph) must first be taken into account before we decide that increased vesicular breathing is pathologic.

Pathologically, increased vesicular breathing depends most frequently upon a *catarrh of the finer bronchial tubes*. The latter are narrowed by the swollen mucous membrane, and this stenosis presumably causes the increased breathing. This explanation would naturally support the friction theory of vesicular breathing, and would negative Baas' theory.

Another cause for pathologically increased vesicular breathing is the more active breathing of a certain portion of the lung. This happens wherever part of a lung is retracted or relaxed, and is generally accompanied by an abnormally loud or tympanitic percussion note. (See p. 271.) Thus, we frequently hear increased vesicular breathing in *the first stage of croupous pneumonia*, in *the neighborhood of consolidations*, or *in the neighborhood of affections of the thoracic cavity which limit the space*, etc. In pleurisy with effusion and in pneumothorax the respiratory murmur is diminished or absent over one-half of the thorax, despite the pronounced retraction of the lung. But over the other chest half the breathing is *increased* vicariously. The same condition is often noted in pneumonia and in pulmonary tumors.

Increased vesicular breathing is of special importance in demonstrating multiple small areas of consolidation which furnish no other auscultatory or percussion signs. The increase depends partly upon the retraction and relaxation of the neighboring pulmonary tissue, partly upon the accompanying localized catarrh. For this reason increased

vesicular breathing localized over one apex is an important sign for recognizing incipient tuberculosis, and especially so because at the apex, where tuberculosis most frequently makes its first appearance, vesicular breathing is normally weak.

Weakness, diminution, or *absence of vesicular breathing* is observed under manifold conditions. Careful attention should be given to the physiologic variations before we can assume any pathologic changes. Any cause which limits the inspiratory distention of the pulmonary parenchyma will diminish and finally abolish the vesicular breathing, *e. g.*, any obstacle to respiration situated in the larger air-passages. If the obstacle be located in the larynx or trachea, the respiratory murmur will be diminished over both lungs. If located in one bronchus, it will be diminished over the entire pulmonary territory supplied by that bronchus. This furnishes us with a means of estimating the degree of laryngeal stenosis in croup and of determining any extension of the croupous process down into one or the other bronchus. A localized diminution or abolition of the vesicular breathing is important for estimating the position of a foreign body in the bronchus.[1] The respiratory murmur is diminished in certain forms of catarrh which cause an exceptionally marked stenosis of the affected bronchi. The murmur is abolished in obturation atelectasis.

Even if the air-passages be free, diminished breathing will be observed when any sort of mechanical obstruction prevents the normal alveolar distention, *e. g.*, firm pleural adhesions which limit the lung excursions. Multiple small consolidations often diminish or abolish the vesicular breathing because, to a certain extent, they make the intervening portions of the lung, which are still pervious to air, stiff and inexpansible. Increased vesicular breathing is, however, also commonly heard over multiple small consolidations (see above).

Such a localized diminution of the respiratory murmur, whether depending upon a circumscribed catarrh stenosing the bronchi, or upon fixation of the lung by small areas of consolidation, or by pleural adhesions, is very important in diagnosing circumscribed tuberculous areas. Sometimes, though rarely, even a considerable tuberculous consolidation does not show the expected pathologic bronchial breathing, but diminished vesicular breathing. This peculiarity of many tuberculous consolidations, as contrasted with other kinds of pulmonary consolidation, can be explained by the frequent narrowing or contraction of the bronchial lumen in tuberculosis.

Diminished breathing is observed in pleurisy over the affected side, even at the places where the lung lies against the thoracic wall, because either the exudate or the pain limits the excursions of that side.

An emphysematous lung makes very slight excursions, on account of its permanent inspiratory position; hence the respiratory murmur is frequently diminished. But a coincident catarrh of the bronchi will tend to intensify the respiratory murmur, and so the final result will naturally depend upon the factor which is in excess. Diminished breathing is one of the cardinal symptoms of *pleurisy, hydrothorax, pneumothorax,* and *pulmonary tumors,* for two reasons: In the first place, the excursion of the affected side is limited; and in the second place, the transmission of the breathing to the examiner's ear is impaired by the interposition of fluid or solid tissue or of air.

[1] [The *x*-ray will usually settle this point.—Ed.]

VESICULAR BREATHING WITH PROLONGED EXPIRATION

Normally, we hear only a very short, faint murmur or none at all over the lung during expiration. But under some circumstances the expiratory murmur may be increased and prolonged until it lasts even longer than inspiration.

Prolonged expiration is a frequent, though not constant, accompaniment of increased vesicular breathing. It occurs in bronchitis, probably because the swollen mucous membrane opposes an obstacle to the respiratory current, and produces a stenotic murmur with expiration. Expiration, as is well known, is less powerful and slower than inspiration, and the stenosis slows it still more. If the catarrh be localized at certain places, the prolonged expiration also will be a local phenomenon. The prolonged expiratory murmur in the catarrh of emphysema and in asthmatic paroxysms is very pronouced and is diffused over the entire lung. In such cases the expiratory movement of the thorax is in itself prolonged. (See p. 95 et. seq.) Increased and prolonged expiration is a symptom of catarrh; and, therefore, if it be localized, it has the same significance in the diagnosis of diseased areas (consolidation, tuberculosis) as has localized increased or diminished vesicular breathing (pp. 285 and 286).

F. Müller has, however, called attention to the fact that the normal expiratory murmur over the right apex is frequently increased or prolonged in comparison with that over the left. This coincides with the greater distinctness of the physiologic bronchial breathing on the right side. (See p. 284.) If this fact be not kept in mind, a false diagnosis of tuberculosis may be made. On the right side, therefore, only very considerable variations from the normal should be given weight, especially if other signs (dulness, râles, retraction) be absent.

ROUGH OR IMPURE AND COG WHEEL VESICULAR BREATHING

Rough vesicular breathing is an impure, slightly uneven murmur, heard during inspiration, as if strange accompanying noises were admixed with the normal vesicular murmur. In order to prevent confusion with sharp or increased vesicular breathing (p. 285), the term impure breathing should be used. Increased breathing is exquisitely pure and generally very intense, whereas rough breathing is more frequently faint and indistinct.

Impure as well as increased breathing is a sign of bronchial catarrh, and may or may not be accompanied by prolonged expiration. Either the partial impermeability of the bronchi produces unequal respiratory excursions of the lung area in question, or else accompanying noises derived from the presence of secretion are mixed with the pure vesicular murmur. If these accompanying noises can be plainly isolated, we call them *râles* (see p. 293), but if they remain indistinct and blended, the vesicular breathing becomes impure or rough.

The so-called *cog-wheel respiration* resembles impure breathing, but is characterized by jerky, intermittent pauses in the inspiratory murmur or by accompanying noises which plainly separate the individual portions of the murmur from each other. In contrast to impure breathing, these individual portions retain their smooth sighing or sipping character. The acoustic peculiarities of cog-wheel respiration convince us that it is caused by the air-current being forced into the alveoli with effort and intermittently overcoming some obstacles. Cog-wheel respiration localized over a definite area of the lung is also a sign of catarrh,

and it is natural to assume that such intermittent obstruction to the respiration is due either to valve-like swellings of the mucous membrane or to accumulations of secretion which must be pushed aside by the air-current. Hence its relationship to impure or rough breathing. Naturally, cog-wheel inspiration may also be an increased or diminished breathing and may be associated with prolonged expiration. Sometimes the expiration is also cog-wheel in type.

Hensen[1] has called attention to the fact that in many cases of cog-wheel breathing the intermissions are synchronous with the pulse (*pulsating cog-wheel breathing*). He explains this phenomenon by the supposition that hyperemia of the lung is responsible for this form of cog-wheel breathing, the pulsation of the pulmonary arteries rhythmically decreasing and increasing the respiratory movements. This pulsating character, however, may be explained equally well by the previous statements if we bear in mind that every systole of the heart lowers the intrathoracic pressure and, consequently, through the mechanism of the systolic vesicular breathing (see p. 284), accelerates the inspiratory air-current. The latter explanation ought, then, to apply to those cases in which the pulsating cog-wheel breathing is audible only in the neighborhood of the heart. It is also conceivable that even in the absence of pulmonary hyperemia the pulsation of the pulmonary arteries may give to ordinary cog-wheel breathing, caused by an obstacle in the smaller bronchi, a rhythm synchronous with the pulse. C. Gerhardt maintains that insufficiency of the pulmonary valves may cause pulsating cog-wheel breathing by the systolic expansion of the arteries of the lung arising from the pulsus celer.

There is another kind of cog-wheel respiration not at all dependent upon the pulmonary, bronchial, or cardiac condition, but upon uneven or intermittent action of the inspiratory muscles. This occurs by no means rarely in partial paralyses and during fatigue of the respiratory muscles. It can be distinguished from the form described above by its more even distribution over the entire lung and by the fact that it is not synchronous with the pulse.

PATHOLOGIC BRONCHIAL BREATHING

Pathologic bronchial breathing is a blowing murmur heard over morbid areas, and is practically identical with the sound we have already described under the term physiologic bronchial breathing, *i. e.*, with a laryngotracheal murmur resembling the syllable "ha." From experience we have learned that it is to be heard wherever the pulmonary parenchyma is airless (whether on account of external compression or on account of consolidation), wherever there are pathologic pulmonary cavities which freely communicate with the bronchus, and wherever a diffuse or sacculated dilatation of the bronchi exists.

One of the oldest explanations of the origin of bronchial breathing over solid portions of the lung assumed that the vesicular breathing disappeared and that the laryngotracheal murmur was transmitted more plainly to the surface of the thorax through the thickened lung parenchyma than through the air-containing tissue. But this explanation is not tenable, because we can prove that a solid organ does not transmit this murmur so well as does the air-containing lung. However, although the hepatized tissue itself does not transmit the laryngeal murmur better than the normal lung, nevertheless the air-containing bronchi incased in a solid tissue are better conductors than when incased in air-containing tissue.

This modified explanation is to-day rather generally accepted, but it, too, is insufficient, for in pneumonia bronchial breathing is heard not only over the consolidated area, but also in its vicinity and upon the opposite (healthy) side in the neighborhood of the spinal column. With such a result we sometimes erroneously diagnose a double pneumonia, and learn at the autopsy that the bronchial breathing must have been

[1] Arch. f. klin. Med., 1902, vol. lxxiv, p. 237.

transmitted from the affected side. This transmission of bronchial breathing shows how imperfect the preceding theory is, for it demonstrates that bronchial breathing can be very well transmitted to a distance in air-containing tissue. If, then, the bronchial breathing be really as intense in the normal bronchi as in the infiltrated tissue, how can we explain why in sound lungs it should not be able to reach the examiner's ear? The vesicular breathing certainly does not conceal the bronchial breathing, because both in transmitted bronchial breathing and also under other circumstances (mixed breathing, see p. 284) we can appreciate at the same time both a bronchial and a vesicular murmur. The author explains the transmission of bronchial breathing through healthy portions of the lung in the neighborhood of a consolidation by assuming that the consolidated lung not only transmits the laryngeal murmur to the surface through the bronchi, but magnifies it. It is evident that such an increase in a portion of the lung immovable on account of the consolidation would be produced best by resonation or consonation (Skoda). The variations observed in the pitch of bronchial breathing (p. 270) show that real resonating phenomena can appear in the bronchi of consolidated portions of lung. This question of resonance will be discussed under Consonating Râles.

Fig. 151 explains another cause of the increase of bronchial breathing over consolidated areas. Here *a b c d* represent a consolidated, *a f e d* a non-consolidated, bronchial area, with the tributary bronchi *g h* and *g i*. As a consequence of the consolidation the air-current between *h* and *g* ceases, whereas that from *g* to *i* persists, so that at the point *g* the current conditions are decidedly altered. The current of

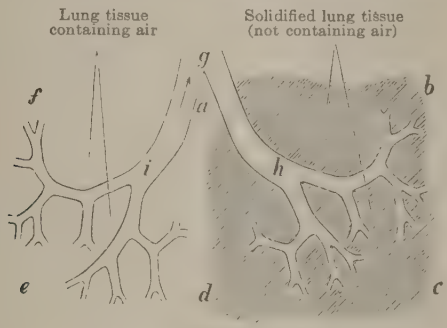


Fig. 151.

air *i g* blows over a quiet column of air and might very likely produce bronchial breathing similarly to the noise made by blowing over the opening of a key

Pathologic bronchial breathing is sometimes, although rarely, heard louder during inspiration, and not, as is the laryngeal murmur, during expiration. This fact, it seems to the author, argues in favor of the last-mentioned theory of the origin or increase of bronchial breathing, and cannot be explained by mere conduction and resonation.

The result of this discussion should lead us to conclude that better transmission of the laryngotracheal murmur is not sufficient to explain the presence of pathologic bronchial breathing over pulmonary consolidation, but rather that the laryngotracheal murmur comes much better to the surface in solid tissue with open bronchi, and that in the thickest portions it is even intensified.

There is no appreciable acoustic difference in the bronchial breathing whether the pulmonary consolidation consists in an infiltration of the alveoli with inflammation products, or in an atelectasis from compression of a pleuritic exudate, pneumothorax, hydrothorax, or pericardial exudate. Naturally, this compression of the lungs must be limited to the alveoli alone and not involve bronchi, at least not those of any size. For as soon as an effusion, for example, increases enough to compress the larger bronchi, the bronchial breathing, which is frequently heard with

difficulty on account of the interposition of the effusion, becomes fainter and fainter and finally disappears.

Obturation atelectasis, due to the plugging of a bronchus and a consequent resorption of air from the alveoli, prevents the production of bronchial breathing, and in spite of the pulmonary consolidation and of the consequent dulness, no respiratory murmur can be heard unless it be transmitted from the neighborhood.

Even very tiny areas of consolidation, too small to dull the percussion-note, may cause bronchial breathing. This shows how valuable a sign it is in diagnosis, and is another argument against the transmission theory of bronchial breathing.

Bronchial breathing is also heard over pathologic air-containing cavities which communicate with the bronchi, and over dilatations of the bronchi themselves. Here it is probably due to a better transmission of the laryngeal murmur, especially if the cavity or the bronchiectasis lie superficially. Besides, such cavities are almost always surrounded by consolidated tissue, so that resonance contributes considerably to the increase of the laryngeal murmur. Finally, we must not forget that under some circumstances a cavity itself breathes, *i. e.*, a respiratory current of air streams through the entrance of the cavity into the bronchus and back again. And this would cause a blowing respiratory murmur, just as in the larynx.

Sometimes it requires very deep respirations to make the bronchial breathing audible. Again, closure of the bronchus, *e. g.*, by secretion, will interrupt the bronchial breathing. Hence, sometimes after coughing the bronchial breathing will reappear. A good device for bringing out faint bronchial breathing, if a patient cannot be persuaded to breathe deeply, consists in having the patient count aloud as long as possible during one respiration, while the examiner auscultates. The next inspiration will be a maximum. This method has also the advantage of demonstrating bronchophony. (See p. 302.) The ear applied directly to the chest will sometimes appreciate faint bronchial breathing better than with the interposition of the stethoscope (p. 281), especially in the case of young children. It is advantageous to close the other ear with the finger.

DIFFERENT KINDS OF PATHOLOGIC BRONCHIAL BREATHING

Bronchial, far more than vesicular, breathing has a definite pitch (p. 288), which may vary quite decidedly. These variations can easily be reproduced by fixing the mouth in the position for saying the syllables "ha," "he," "hi," "ho," "hu," and then inspiring and expiring.

The pitch of bronchial breathing depends in certain cases upon the conditions of resonation, and with them upon the width of the bronchi or of the cavities. But up to the present time, except perhaps in distinguishing so-called amphoric breathing, the pitch has not occupied an important place in diagnosis. By *amphoric* or *cavernous* breathing we mean a very deep and soft and generally not very loud bronchial breathing, heard especially over large cavities containing air (lung cavities and pneumothorax). Besides its low pitch it has a very characteristic metallic quality, apparently due to the high overtones from the resonance in the cavity. Amphoric breathing is, therefore, sometimes associated with a metallic percussion-note. We may produce it

by whispering the syllable "hu" or by blowing over an empty jar; whence the name. Provided that we do not call every deep bronchial breathing *amphoric* (a frequent mistake), amphoric breathing is a pretty sure sign of a cavity. The metallic resonance accompanying it is confirmatory evidence. Like metallic percussion, amphoric breathing excluding that found in pneumothorax arises, for the most part, only over cavities which are at least 6 cm. in diameter (according to the ordinary estimate); but it is sometimes found over smaller cavities.

Amphoric respiration may be heard over a pneumothorax from resonation if, as is most common, it be a closed, or valve, pneumothorax.

The pitch of amphoric breathing, *i. e.*, of its metallic resonance, may vary in accordance with laws similar to those governing the metallic percussion resonance. (See the paragraphs upon the Change in Percussion-note, p. 275 et seq.)

Metallic breathing is to be distinguished from amphoric breathing. It is a murmur with high metallic overtones and without the deep basal tones. If a basal tone be audible at all, it is high, not deep. Metallic breathing may be heard over consolidation, provided the conditions are favorable for resonance, and particularly over small pathologic cavities or dilatations of the bronchi.

The respiratory murmur may in rare cases assume an amphoric or metallic character on account of the resonation set up in neighboring physiologic air-containing cavities, such as the stomach or the distended intestines.

In marked dyspnea certain positions of the open mouth may add an amphoric resonance to pathologic or physiologic bronchial breathing. But such amphoric breathing can be appreciated at a distance, and, besides, is distributed exactly like physiologic bronchial breathing, so no confusion need result. Moreover, it disappears when the mouth is closed.

METAMORPHOSED BREATHING MURMUR

Metamorphosed breathing is essentially bronchial in type. In the more common form inspiration begins sharp, blowing, and bronchial, gradually becoming much softer, and sometimes ending in amphoric breathing. In another variety the pitch of the bronchial element changes during inspiration or during expiration or during both. Either type, if heard continuously, is a practically sure sign of a cavity, provided it persists. Probably after the inspiration has lasted for a certain time it distends the cavity and its orifice enough to modify the pitch of the respiratory murmur. The author once succeeded in demonstrating two different metamorphosed breathing murmurs over adjacent areas (one higher during inspiration, the other deeper), and in making a diagnosis, which was later confirmed by autopsy, of two small abscess cavities situated near together. A similar but transitory metamorphosed breathing murmur might arise even without the existence of a cavity if the inspiratory current pushed aside the secretion of a partially occluded bronchus. Laënnec's "souffle voilé" is another variety. It begins as vesicular and then changes into bronchial or mixed breathing. (See p. 292.) The vesicular element in this case is probably transmitted. (See p. 292.) It occurs principally over tuberculous consolidations.

INDEFINITE BREATHING MURMUR

This is neither vesicular nor bronchial, but sounds like the expiratory portion of normal breathing. The term indefinite is applied also to breathing which is very faint and difficult to hear. Both bronchial and vesicular breathing may be diminished enough by a pleural exudation to become transformed into indefinite. Sometimes the breathing becomes indefinite because it is masked by other louder noises (râles or friction sounds). The true nature of indefinite breathing can often be brought out after the patient breathes deeply. Loud, distinct breathing is never indefinite, nor is the mixed murmur (to be described below). The only diagnostic significance of indefinite breathing is that of a very weakened murmur whose vesicular, bronchial, or mixed origin cannot be determined.

MIXED BREATHING MURMURS [BRONCHOVESICULAR BREATHING.—ED.]

There are two main types of mixed [bronchovesicular.—Ed.] breathing:

1. Vesicular inspiration with bronchial expiration.
2. Mixed inspiration, *i. e.*, inspiration which is both vesicular and bronchial, with bronchial expiration.

The conditions of origin of bronchial and of vesicular breathing differ so manifestly that, at first sight, it would seem difficult to explain these mixed murmurs. Practically, however, the vesicular and bronchial elements never arise from one spot, but each is transmitted from some distance and heard in combination with the other; and so a mixed murmur entitles us to assume that there exist in close proximity both normal pulmonary tissue and tissue so altered as to produce bronchial breathing. Thus, mixed [bronchovesicular.—Ed.] breathing is to be heard: (*a*) over portions of the lung containing scattered small consolidations; (*b*) over normal pulmonary tissue near large consolidations; (*c*) in the neighborhood of the upper boundaries of dulness of a pleural effusion which compresses the inferior while permitting free breathing of the superior portion of the lung; (*d*) over cavities surrounded by healthy lung tissue, etc. The importance of mixed [bronchovesicular.—Ed.] breathing in disclosing small areas of consolidation is evident, because such areas need not produce any dulness.

Physiologic bronchial breathing is almost always combined with vesicular breathing. This is important in differentiating physiologic from pathologic bronchial breathing. But the latter may also be mixed with vesicular breathing, and the distinction between physiologic and pathologic mixed breathing is as difficult as it is important. Physiologic mixed breathing is especially common over certain areas, mentioned above (see p. 284), whereas pathologic mixed breathing may be heard over any part of the lung. Even where physiologic mixed breathing is diffused over a large area, we can easily determine that the nearer we listen to the greater bronchi or the roots of the lungs, the stronger the bronchial element becomes; and, conversely, the farther from them, the weaker. If the bronchial element increase with the distance from the lung roots, we may infer that it is pathologic mixed breathing. Physiologic mixed breathing is much more affected by the intensity of the laryngeal murmur and by the position of the mouth than is

pathologic. The character of bronchovesicular breathing often varies at different examinations, being at the one time plainly vesicular, at another, bronchial. This is supposed to be due to secretion plugging a bronchus, at one time in the consolidated area, at another in the normal area. In the former case the bronchial, in the latter the vesicular, component is weakened or disappears.

There is still another type of mixed breathing which is of diagnostic importance. Mixed breathing is sometimes heard over a considerable area of the lung, loudest near the hilum (physiologic type); or, conversely, near the pulmonary edges. If accompanied by a chronic cough, but with no other evidence of pulmonary infiltration or tuberculosis, it would argue very strongly for diffuse bronchiectasis.

The device for recognizing weak bronchial breathing (p. 291 et seq.) also aids in differentiating mixed from pure vesicular breathing.

RÂLES (Rhonchi)

Under this term are included all sounds which are caused by the motion in the bronchi, not only of air, but of secretions or of other fluid, semifluid or solid materials. Such motion may be caused either by breathing or by coughing. Moist râles depend upon fluid; dry râles upon solid, material within the bronchi. To determine râles exactly and to analyze them carefully we must auscultate the patient during deep as well as during quiet breathing, and also during and following a cough. No other auscultatory phenomenon are so markedly altered by such a variation in the type of examination. Coughing, for instance, will oftentimes cause râles either to appear or disappear. If a patient be difficult to examine, if he cannot be persuaded to breathe properly, tell him to count aloud as long as possible, without taking breath, and the next inspiration will naturally be full and deep. We can often bring out a very few râles, the demonstration of which over the pulmonary apices is very essential in the diagnosis of pulmonary tuberculosis, by auscultating the patient early in the morning, before he has expectorated the secretion accumulated during the night. Examination should be made with the patient in different positions. Râles can often be felt by the hand placed upon the chest.

Transmission of Râles.—Râles can also be heard by transmission at some distance from their place of origin. But their intensity ordinarily decreases so quickly that the determination of their origin rarely offers difficulty.

Oral Râles.—It frequently happens that râles may be heard at some distance when the patient breathes with his mouth open. In general these râles are so intense that they can often be heard at a distance even with the mouth shut. This transmission of râles through the mouth is particularly marked in the tracheal and pharyngeal râles of moribund patients. These râles owe their origin to the flooding of the bronchi, trachea, and pharynx by the fluid of the pulmonary edema, but, in the case both of moribund patients and of those afflicted with esophageal paralysis, may also be caused by failure to swallow the pharyngeal or laryngeal mucus. By auscultating and palpating the trachea and the larynx, it may be determined whether the râles arise here or in the depths of the lung. Owing to peculiar conditions for resonance, it occasionally happens that a deep area in the center of the lung produces oral râles which are not transmitted to the surface of the thorax. This symptom has a certain diagnostic significance.

MOIST OR BUBBLING RÂLES

The sound of moist or bubbling râles can be imitated by blowing through a glass tube into a vessel of water. The bursting of the air-bubbles causes a characteristic crackling noise, which varies with the caliber of the tube and with the strength of the bubble. A wide tube produces large bubbles, with a sound resembling the so-called *large* or *coarse bubbling râles;* a narrow tube causes fine bubbles, the sound resembling the *small* or *fine bubbling râles.*

It is much easier to appreciate by the ear the difference between the fine and the coarse bubbling râles than it is to define it scientifically. *Coarse bubbling râles* are fewer in number, more intense, and of a lower pitch. *Fine bubbling râles* are more numerous, less intense, and of a higher pitch. This distinction does not, however, entirely fulfil the conditions, because accelerating the air-current in the experiment mentioned above increases the number of the bubbles without altering their character. On the other hand, holding the ear close to or distant from the tube will increase or diminish their intensity also without altering their character. Neither does the essential distinction depend upon the pitch, for with many râles no distinct pitch can be recognized. Therefore, some other difference between coarse and fine bubbling râles must exist. The author imagines the difference depends in part upon the size of the mass set in motion, *i. e.*, in coarse bubbling râles the energy of the vibration is greater than in fine bubbling râles, because the moving mass is larger. And this influences not only the intensity of the vibrations, but, in consequence of the law of inertia, the duration of the tone itself. The coarse râles last longer. (See Duration of the Percussion-note, pp. 203 and 207.) If this explanation be correct, râles may be few in number, and, when they arise close to the ear, intense, and yet retain their fine bubbling character.

The term "bubbling" was employed because it was formerly supposed that moist râles arose from the bursting of air-bubbles in fluid secretion. Of course, we know now that the contents of the bronchi are not sufficiently fluid nor abundant for such an explanation; and so we suppose that the râles arise when membranes of secretions are formed in the bronchial lumen, are stretched and then torn apart again, partly by the movement of the air and partly by the movement of the lungs. The *coarse bubbling râles* would therefore correspond to the thicker, and the *fine* to the thinner, layers of secretion. We always auscultate over a more or less extensive bronchial area; hence many different individual noises may give rise to the resultant "much bubbling" noise even if in single bronchi there be only isolated bubbles. The bursting of real bubbles probably occurs only in quite rare cases, and then really only when the lung is saturated with thin fluid, *e. g.*, in pulmonary hemorrhage, pulmonary edema, or drowning.

Moist râles may be heard during expiration as well as during inspiration, although during inspiration they are almost always much plainer, possibly because the movement of the lung is then normally quicker.

Very fine bubbling or moist râles are also named *crackling*, or better *subcrepitant râles*, the latter from a certain similarity to *crackling râles* or *crepitation*. The choice of terms and the distinction between the two are thoroughly discussed upon p. 298 et seq.

A complete series of transitions exists between the coarse bubbling

râles as one extreme and the fine subcrepitant râles as the other. The rattling tracheal or pharyngeal râle, generally heard in the moribund, even at a distance, belongs to the former variety. (See p. 293.) Fine moist râles more commonly originate in the fine tubes; coarse, in the larger tubes or in pathologic cavities. The former are generally more numerous because there are more fine tubes.

Moist râles arise only when the bronchi contain fluid or semifluid material; in most cases, therefore, they signify a bronchial catarrh, located in the large or small bronchi, according to the size of the râles. Fine moist râles have in general a more serious import, because a catarrh of the finer bronchi often leads to bronchopneumonia, and because such a catarrh frequently depends upon local changes of the pulmonary parenchyma (such as inflammatory consolidation, tuberculosis, or infarction). This is especially true if the fine moist râles be localized over a definite area of the lung. The obstinate persistence of such localized râles over the same area while the rest of the lung is permanently free, without any other signs, justifies the diagnosis of a serious process, either a tuberculous or a lobular pneumonic consolidation or an infarction. On the contrary, an ordinary innocent catarrh is much more diffused, because an otherwise healthy mucous membrane presents practically the same fostering soil throughout its entire extent. Coarse bubbling râles heard over areas where no large bronchi are to be found signify an especially serious affection, because they must arise either from pathologically dilated bronchi or from cavities. When heard over the apices, they are thus important signs of tuberculous cavities; when heard over the postero-inferior portions of the lungs, they more frequently depend upon bronchiectasis. Coarse moist râles are, however, frequently transmitted to quite a distance, a possibility which must be kept in mind when they are heard over areas somewhat remote from the roots of the lungs. Such a possibility may, however, be excluded if, at the same time, no coarse râles be heard over the larger bronchi. Moist râles of any size, when obstinately localized over a circumscribed area, point to a serious focal lesion of the lungs.

Mixed bubbling râles arise when the small as well as the large bronchi are affected. They may also arise from the larger bronchi and from pulmonary cavities without the smaller bronchi being affected, since, as has been mentioned, fine as well as coarse bubbling râles may be formed in the larger vessels and cavities.

Pulmonary hemorrhage and pulmonary edema, unless the larger bronchi are also flooded with fluid, present quite uniformly fine bubbling râles, which are frequently heard with both inspiration and expiration (continuous râles). The expectoration in these cases is ordinarily very foamy. If the larger air-passages be flooded also, coarse râles are mixed with the fine, and oral râles are often heard. (See p. 293.)

The sticky mucous secretion of an ordinary catarrhal bronchitis generally produces *dry* râles. Moist râles have a more serious significance; their appearance is associated with a fluid secretion deficient in mucus, *e. g.*, they are especially common in intense inflammatory processes of the mucous membrane or of the pulmonary tissue, in edema, stasis, and hypostasis. Moist râles constantly present over the apices of the lungs almost always mean tuberculosis. In such a case a thin fluid secretion, such as the moist râles suggest, signifies a marked purulent and destructive process.

DRY RÂLES (CRACKLING OR SNAPPING AND MUSICAL RÂLES

Dry râles are produced by the movement of a viscid secretion. They have a more manifold character than moist râles. The latter are always composed of a more or less regular succession of separated noises. The former present either a quiet, isolated sound, a crackling which resembles to some extent a moist râle, or a prolonged, distinctly musical sound (musical râles). The difficulty in moving the tenacious secretion probably accounts for the lack of regularity in the succession of the dry râles.

To explain the origin of the *crackling dry râle*, we should remember that the secretion of the mucous membrane of the bronchi is stretched out in the form of threads or bladder-like membranes, is torn loose either by the air-current or by the movement of the lungs, and later, by virtue of its tenacity, again sticks fast to another portion of the bronchial wall without necessarily giving rise to another series of noises. Thus, they differ very slightly in their origin from the moist râle, except that on account of its viscidity the secretion is probably only seldom stretched and then torn loose from the mucous membrane, whereas in moist râles this process is constantly repeated. Such a conception practically tabulates the dry crackling râle as a subdivision of the moist râle.

Very possibly certain forms of crackling râles are not real râles, *i. e.*, they do not depend upon the movement of secretion, but upon a jerky current of air over a surface roughened and irregular from infiltration in the neighborhood, *e. g.*, in tuberculous apices.

Musical dry râles arise from the vibration of threads or membranes which are drawn out across the bronchial lumen. They are set in vibration (but not torn away by the air-current), just like the strings of a fiddle or the tongues of a pipe. Again, the walls of some of the finer tubes may be so swollen by inflammation as almost to occlude them and form a sort of whistle. Finally, the swelling of the mucous membrane may be situated at the angle between two communicating bronchi, thus acting like the tongue of a pipe. These various causes explain the diversity of musical râles, which sometimes resemble the purring of a cat, sometimes the tone of a violin, a harp, or a bass viol, sometimes the snoring of a sleeper, sometimes a shrill whistle. All these different varieties may occur simultaneously. The deeper sonorous râles generally arise in the larger bronchi; the higher, whistling or sibilant râles, in the smaller.

The names crackling, sonorous, or sibilant râles—more briefly, crackles, snores, or whistles—appropriately describe the sounds.

When dry râles are obstinately localized at one spot, they have the same serious significance as moist râles, even without other auscultatory or percussion phenomena. (See pp. 294 and 295.) Pulmonary tuberculosis for a long time may be evidenced only by the sounds of a dry catarrh at one apex.

Dry râles are often transmitted to a considerable distance. Sonorous râles are often appreciated by the palpating hand, and resemble a pleuritic friction. (See p. 300.)

RESONANT (Consonating) AND NON-RESONANT (Non-consonating) RÂLES

Râles which arise in bronchi surrounded by solid, *i. e.*, airless, tissue (consolidation, atelectasis) or in pathologic cavities, are transmitted, intensified, or modified by resonance, exactly as is pathologic bronchial breathing. (See p. 288 et seq.) They can become exceptionally sharp and distinct, and are called *resonant* or *consonating râles*, in distinction to the non-resonant râles heard over normal pulmonary parenchyma. The terminology is here somewhat confusing, for a dry musical râle must naturally be resonant, but is not modified by a resonance in the sense mentioned above. To avoid this confusion it is advisable to return to Skoda's term, *consonating râles*.

Dry musical râles (sonorous and sibilant), even when they arise in aërated pulmonary tissue, have so distinct and well recognized a musical character that conditions of resonance or consonance cannot alter them to any extent, and only a very skilled ear can distinguish any difference between consonating and non-consonating musical râles. On account of the marked preponderance of a ground-tone, consonance in such râles is evidenced more by an increased intensity than by any qualitative modification of the timber. Merely from the increase in intensity, we can draw no further conclusions. But moist and also *crackling râles* are very plainly affected by consonation. The entire effect is increased in intensity, and certain high partial tones are especially intensified by resonance. The result is difficult to describe clearly, but can easily be demonstrated upon an appropriate patient. In the discussion of bronchial breathing we showed that actual resonating phenomena do appear in the bronchi, and so there is no reason to doubt that a râle may resonate. But the better conduction through consolidated tissue is not alone sufficient to make the râles resonant; nor is loudness of any avail, for tracheal râles loud enough to be heard even at a distance show no trace of resonance. The resonating character depends, for the most part, on an admixture of the higher overtones. Certain types of stethoscopes will add a distinct resonance to râles. (See pp. 280 and 305.) A pulmonary cavity which presents a metallic note to percussion and an amphoric and metallic breathing to auscultation also furnishes consonating râles, with a metallic resonance.

The so-called metallic tinkle (gutta cadens), heard especially in tuberculous destruction of the lung, is apparently nothing but a metallic consonating crackling râle in a cavity (see, however, a similar sound with a different import, p. 302, Pneumothorax). After this discussion of its origin, the diagnostic significance of the consonating râle will require fewer words, for it should now be clear that the demonstration of the consonation of râles has exactly the same significance as the demonstration of pathologic bronchial breathing. And the author would emphasize to the beginner the importance of distinguishing consonance and non-consonance of the râles in the diagnosis of consolidations. If bronchial breathing, consonating râles, and dulness of the percussion-note were always present together over pulmonary consolidations, the presence of one or the other of these signs would be sufficient, and we could then dispense with the others. Unfortunately, it is not so simple; for, as we have already seen, bronchial breathing is very often heard without any dulness, and just as frequently there are consonating râles without bronchial breathing. Roughly, the con-

ditions essential for consonating râles and for bronchial breathing are the same; but either may be present alone, because quite distinct sound elements must be increased by resonation to exhibit the consonating character in the râles, on the one hand, and in the respiratory murmur, on the other.

From a practical standpoint there is one thing more to emphasize. A râle must possess a certain strength to be able to consonate plainly; hence, with very superficial breathing we frequently hear over a consolidation or a cavity non-consonating râles, which, with deeper breathing, are transformed into consonating râles. Lobular pneumonia is often very difficult to demonstrate in quite sick patients, especially because the superficial breathing characteristic of this disease is scarcely strong enough to produce plain bronchial breathing. With mixed bubbling râles certain ones may be consonating and others non-consonating, because parts of the mixed breathing murmur are not strong enough to bring out the consonation.

CREPITANT RÂLES OR CREPITATION

During the first stage of croupous pneumonia, when anatomically the lung is in the state of engorgement, when the pulmonary tissue is still full of air, when percussion discloses no dulness, and when auscultation shows no bronchial breathing, there is to be heard over the affected part of the lung the so-called *crepitant râle*, or *crepitation* (crepitatio indux). A similar noise (crepitatio redux) is to be heard during the resolution stage of pneumonia when the solidified lung again becomes aërated. This characteristic sound is to be heard both in *croupous* and *catarrhal pulmonary inflammation*, in certain stages of *tuberculous infiltration*, in *hemorrhagic infarctions*, and in *beginning pulmonary edema*. In most cases only audible during inspiration, *crepitation* possesses a certain acoustic similarity to a very fine moist râle (subcrepitant), and can be very well imitated by rolling one's hair between the fingers, near the ear.

Formerly, crepitation was considered to be a true, very fine, moist râle, arising when the air-current set into motion fluid secretion in the finest bronchi and alveoli. But this supposition has been disputed; in the first place, because we can reproduce crepitation by blowing up or by pressing between the fingers the absolutely dry lung of a cadaver; and again because in perfectly healthy individuals, with no real secretion in the alveoli or bronchi, crepitation is sometimes heard after they have been breathing superficially for a long time and then take a deep breath. The fact that it is heard only with inspiration is a further argument against its origin from the movement of secretion. It is now apparently universally conceded that crepitation does not arise from this cause, nor, as was earlier supposed, as a consequence of a great number of microscopic explosions of air-bubbles in the fluid contents of the alveoli, but from the tearing apart of the approximated alveolar walls by the inspiratory stream.[1] In pulmonary engorgement related to the first stage of pulmonary edema we can well imagine that the increasing swell-

[1] [Prof. Sahli has entirely disregarded one theory of the origin of crepitation, viz., that it is in reality a very fine pleural friction rub and does not come from within the lung. So good an authority as Osler says, "Whether this is a fine pleural crepitus or is produced in the air-cells and finer bronchi is still an open question."—Ed.]

ing and soaking of the alveolar walls would approximate them, and the presence of some fluid secretion or exudation in the alveoli would only favor each expiratory adhesion. Still, fluid plays here a secondary rôle. In pulmonary edema, if the transudation increase, genuine fine bubbling râles become gradually associated with crepitation, and later on, when the fluid reaches the greater bronchi, even coarse moist râles are developed. An excellent opportunity is thus afforded to study the difference between crepitation and the fine moist, or so-called subcrepitant, râles. They are easily distinguished by remembering that the former occurs during inspiration and possesses a resonating character.

When associated with bronchial breathing, crepitation points to the beginning of a consolidation, and has, therefore, a serious significance. On the contrary, however, the crepitatio redux at the termination of a pneumonia is a longed-for sign of beginning resolution, and a demonstration that the alveoli have once more become permeable to air. Crepitation may in certain cases be heard over some spot or other of the chest during the entire course of croupous pneumonia, because this disease almost never develops simultaneously at all points.

In making a diagnosis, the existence of the above-mentioned physiologic crepitant râles at the borders of the lung must be remembered. When there is but little need of air, the lungs are not freely expanded, so that the alveoli at the borders of the lung may become empty through compression. If, then, the patient be made to take several full breaths, the air rushing into the collapsed alveoli may cause crepitation. These physiologic crepitant râles appear only near the borders of the lungs, usually occur symmetrically on both sides, especially in front, and disappear after a few deep breaths. They may be further differentiated by the absence of any other abnormal signs at the spot in question.

Actual crepitation may exceptionally be heard with expiration, probably depending upon the fact that under usual conditions some of the alveoli become filled with air during expiration instead of during inspiration. This is simple enough to understand if we suppose that, in consequence of adhesions or of partial rigidity from small areas of consolidation, one portion of the lung does not breathe so well as an adjoining part, and that the part breathing well may, on account of some obstacle opposing its emptying (secretion or swelling of the mucous membrane), sometimes pump the expiratory air into the part breathing poorly. The latter will then be distended while the rest of the lung expires, thus giving rise to a crepitation which is expiratory in relation to the general respiration, but inspiratory in relation to the affected part itself. In lobular consolidations at the sharp pulmonary edges the author has not infrequently found this expiratory crepitation.

CARDIOPNEUMATIC RÂLES (Cardiac Râles and Cardiac Crepitation)

Before concluding the discussion of the ordinary râles occasioned by respiratory movements, we should mention the fact that in rare cases with coexistent catarrh of the bronchi, râles may be produced by the movements of the heart itself. These are due in part to the direct mechanical vibration of the adjoining portions of the lung; in part, however, to the systolic and diastolic variations of intrathoracic pressure from alterations in cardiac volume (auxo- and meiocardia). Such variations cause real respiratory excursions of the adjoining pulmonary

parts. (Already noted under Systolic Vesicular Breathing, pp. 284 and 288.) Cardiac râles are most frequently systolic when the lung, partly consolidated or filled with cavities, is adherent to the pleura near the heart, and then set into active motion by the cardiac action.

In a similar way, provided the essential characteristics are present in the lungs, *crepitation* may be occasioned by the heart action (cardio-systolic râles).

PLEURAL FRICTION SOUND

The two pleural surfaces move against each other normally without producing any noise; but when the surfaces have become roughened, as in pleurisy, in tuberculosis, in tumors, or with the abnormal pleural dryness of cholera, a characteristic friction sound is developed. The area over which the friction sound is audible varies with the extent of the fibrinous deposition or roughness. The excursions of the pleural surfaces are more extensive at the pulmonary edges; therefore, a friction sound is more often heard there than at the hilum of the lung. Friction sounds are rarely heard over the apices of the lungs, where the movement is more a distention by centrifugal inflation than a sliding. Depending upon the type of roughness, the rub will be either inspiratory or expiratory, or both. The kind of noise produced is practically manifold. It may be imitated by placing the flat of the hand against the ear and slowly rubbing the back of the hand with the ball of a finger of the other hand. The character of the rub varies with the amount of pressure. Some, exceptionally loud, simulate the creaking of new leather or sonorous râles, whereas others, much fainter, resemble the noise caused by rubbing two pieces of silk cloth together, and still others resemble crepitation, certain râles, cog-wheel breathing, or even faint bronchial breathing. Another peculiarity of friction sounds is that they are usually jerky and not smoothly spread over each phase of the breathing.

Though a mere beginner recognizes without difficulty a decidedly rough pleuritic rub, yet even an expert is sometimes in doubt over the nature of a sound which resembles a sonorous or crackling râle as much as it does a friction. One way of determining is to try the effect of coughing. It will often entirely change the character of a râle, and sometimes even cause it to disappear, but does not affect a rub. On the other hand, pressure of the stethoscope or of the flat hand intensifies a rub, but does not affect a râle. A third source of help is palpation, which appreciates a rub more readily than a râle. [In this connection it is well to bear in mind that we frequently hear subcrepitant râles resembling friction sounds in the lower axillary region of apparently normal individuals. Cabot[1] attributes them to a partial atelectasis resulting from disease of the thin lower pulmonary margin. "Out of 356 normal chests to which I have listened especially for these râles, I found 228, or 61 per cent., which showed them on one or both sides. They are very rarely to be heard in persons under twenty years of age. After forty-five, on the other hand, it is unusual not to find them."—Ed.] The confusion between a soft rub and faint bronchial or cog-wheel breathing can be cleared up only by an expert's repeated and accurate examinations. Another peculiar rub, which, fortunately, is quite rare, can be distinguished from crepitation only by the fact

[1] Physical Diagnosis, fourth ed., p. 163.

that it can be just as plainly heard during expiration as during inspiration, and that it is more jerky than the crepitation. Friction sounds heard over the precordia, which originate from the pleura, from the pericardium, or from the sharp pulmonary edge overlapping the heart, may be synchronous with the cardiac action as well as with the breathing. They are called *pleuropericardial*, *pseudopericardial*, or *extrapericardial friction sounds*, and are liable to be confused with true pericardial rubs. (See Pericardial Friction Sound for Diagnosis.)

In pleurisy with effusion, the friction sound disappears, because the layer of fluid prevents the two pleural surfaces from touching and rubbing. The rub may persist, however, along the edge of dulness, rather more commonly in front than behind. Such a persistence proves that the two pleural surfaces touch and rub against each other somewhere above or below the adhesions, encapsulating the fluid exudate. The reappearance of a rub within the boundaries of the dulness is a favorable sign, because it shows that the fluid is diminishing and the pleural surfaces are again in contact. The dulness may then be due, at least in part, to thick layers of fibrin. Loud friction sounds may, of course, be transmitted some distance from their place of origin; but if they be plainly felt by the palpating hand over the area where they are heard loudest, it is pretty good evidence that they arise very near by.

RESPIRATORY MURMURS IN INTERSTITIAL PULMONARY EMPHYSEMA

When air from within the lung is forced into the interstitial pulmonary connective tissue by the rupture of one or more alveolar walls, bubbling sounds and sometimes murmurs are produced by each respiratory excursion. These sounds generally recall coarse or mixed moist râles, and, for the most part, are resonant in character. The resonance, which may assume even a metallic character, probably depends upon the resonation in the cavities formed by the bubbles. Sometimes these sounds simulate the familiar emphysematous crackling of the skin (see p. 57), but they are too coarse to be confused with crepitation (p. 298 et seq.). When large emphysematous bubbles are situated beneath the pleura, they may sometimes decidedly weaken the respiratory murmur. Interstitial emphysema may be present at any spot; it may spread over the entire lung, and from there in the mediastinum and into the subcutaneous connective tissue. Sometimes the diagnosis of interstitial pulmonary emphysema will be first securely established and the confusion with râles prevented by the demonstration of the precordial murmur of emphysema, and of the characteristic crackling of the skin.

NOISES AUDIBLE IN PNEUMOTHORAX

PLEURAL SPLASHING (Succussio Hippocratis)

Hippocrates first described the characteristic splashing noise produced by shaking a patient with sero- or pyopneumothorax. The noise is similar to that made by shaking a large flask half filled with water, and arises in the same way. Sometimes it is audible at a distance; sometimes only to be heard when the examiner places his ear against the chest. The patient himself frequently notices the noise during all violent movements. The splashing sometimes presents a distinctly metallic timbre, according to the shape and size of the pneumothorax cavity and to the tension of the contained air.

Similar succussion noises may evidently arise in any other physiologic or pathologic body cavity containing both air and fluid; for example, when air is contained in the pericardium or in the peritoneum with a fluid effusion. It is also occasionally heard in a large pulmonary cavity,

and quite frequently in perfectly healthy people with stomachs distended with large amounts of fluid and air. In order to differentiate the Hippocratic succussion in pneumothorax from these phenomena, and especially from the last-mentioned physiologic sound due to the stomach-contents, we must utilize the results of other methods of examination and endeavor to localize the origin of the splashing as accurately as possible by the proximity of the ear, and also by carefully examining with a filled and a fasting stomach. Frequently in pneumothorax the examiner can appreciate, with his hand applied to the patient's thorax, a distinct blow of the fluid wave within the pleural cavity at the moment of the shaking.

WATER-WHISTLE NOISE (Pulmonary Fistula Noise)

This is a characteristic gurgling which often sounds metallic and reminds one of a coarse bubbling râle. It is occasionally heard over a pneumothorax when the air or the fluid is removed by aspiration, and so the atmospheric pressure diminishes the pressure in the pleural cavity. In a valvular pneumothorax the murmur will arise as soon as the pressure within the pleural cavity is diminished to below that of the atmospheric pressure; then air immediately escapes from the patent pulmonary fistula. If this fistulous opening be situated below the level of the fluid, the noise is produced by the rising of the air-bubbles. On account of its acoustic character and of its mode of origin, Unverricht called it a water-whistle noise, and Riegel called it a pulmonary fistula noise. The same noise will be noted even without aspiration if in a patient with a pyopneumothorax perforating into the lung, air be sucked in with inspiration during the expectoration of the exudate, or, again, if with coughing air be squeezed out of the lung by the fluid in a pyopneumothorax which opens through the thoracic wall but is not fully emptied and which also has a pulmonary fistula. The sign is of some diagnostic value in recognizing the occurrence of a pulmonary fistula.

THE NOISE OF FALLING DROPS (METALLIC TINKLE.—Ed.) IN PNEUMOTHORAX

In pulmonary tuberculosis, as we have seen upon p. 298 et seq., the so-called noise of falling drops is always to be considered as a simple metallic crackling râle; but in pyopneumothorax, on the contrary, actual falling drops may be heard. When such a patient changes from the recumbent to the sitting posture, it is quite possible that the shaggy prominences of the pleura covered with fibrin, which were previously moistened, free themselves from fluid drop by drop, and in this way produce a metallic dropping noise.

AUSCULTATION OF THE VOICE SOUNDS OVER THE CHEST; BRONCHOPHONY

Transmission of the voice sounds from the larynx and trachea through the lung to the chest surface is subject, under normal conditions, to the laws which govern the transmission of the laryngotracheal respiratory murmur. The voice sounds are therefore heard best over the areas where we hear physiologic bronchial breathing, *i. e.*, near the hilum of the lung between the shoulder-blades, and over the upper end of the sternum. But even in these regions, under physiologic conditions, no distinct articulation is heard, although when the patient speaks, a strong, sometimes almost fluttering sound is audible. This transmission of the voice is known as *physiologic bronchophony*. The conditions to which it is due are similar to those which cause physiologic bronchial breathing. At best the voice cannot be heard distinctly, but sounds as if some one were talking at some distance in a hall of poor acoustic qualities. The whispered voice is usually heard a little more distinctly. Pronounced bronchophony will at least transmit in-

dividual sounds and the rhythm of syllables. Very faint bronchophony is known as "bronchial whispering or lisping."[1] Physiologic bronchophony decreases rapidly from the region of the larger bronchi toward the peripheral portions of the lung, so that here only an indistinct humming can be detected.

Pathologic bronchophony is similar, acoustically, to the physiologic form. It is due to the same conditions and is subject to the same laws as pathologic bronchial breathing. It is heard over areas of compressed or consolidated lung with patent bronchi, over bronchiectases, and over pulmonary cavities. Bronchophony may acquire a metallic sound over cavities. Pathologic bronchophony, like bronchial breathing, owes its origin partly to better conduction of sound by bronchi which are surrounded by a consolidated area and partly to resonance. Physiologic bronchophony varies in different individuals; hence, in order to detect any pathologic change, it is usually advisable to compare symmetric portions of the chest. It should, however, be remembered that physiologic bronchophony is ordinarily louder on the right side, just as is physiologic bronchial breathing. Both the spoken and the whispered voice should be tested, and the ear which is not used for auscultation should be closed, so as to avoid any sound transmission through the air. Pathologic bronchophony has exactly the same diagnostic significance as consonating râles and pathologic bronchial breathing (see above). All these signs, in virtue of their common origin and uniform significance, may be included in the term "consonating phenomena." Each one should, however, be looked for, because in spite of their uniform cause and significance, any one of the three may be imperfectly developed; bronchophony, especially for the whispered voice [whispered bronchophony.—Ed.] may be heard over a consolidated area, although bronchial breathing is indistinct. If deep breathing be painful or impossible, so that no bronchial breathing can be detected, the demonstration of bronchophony may be of great value.

Extreme bronchophony, or *pectoriloquy*, and *egophony*, a form of bronchophony with a peculiar bleating quality, are sometimes considered as distinct and separate phenomena. But the author does not consider it justifiable to attribute these signs to different conditions, because the various types of bronchophony blend in such a manner as to be indistinguishable one from the other. Neither does he consider it justifiable to attribute any special diagnostic significance to pectoriloquy as a sign of cavities, nor to egophony as a sign of a pulmonary compression which is sufficient to cause flattening of the bronchi. Pectoriloquy may be so decided over a consolidated area that the examiner can appreciate the articulation although he cannot actually distinguish the word. Egophony may also be audible over such an area. All sorts of theories have been suggested to explain the occurrence of the bleating sound in egophony, but none of them has satisfied the conditions from the standpoint of physics. In any case egophony is simply a quantitative increase of ordinary bronchophony and, therefore, cannot depend upon a compression of the bronchi. If the breathing sound amphoric, and if the percussion-note be metallic, the bronchophony is apt to assume either an amphoric or a metallic timbre. By examining for bronchophony with the naked ear, the

[1] [The term "bronchial whisper" should not be confused with "whispered bronchophony."—Ed.]

degree of vocal fremitus can be accurately determined at the same time. In fact, the skin of the ear can appreciate the vibration even more delicately than can the hand, possibly owing to the vibration of the cranial bones.

VARIOUS ERRORS IN PULMONARY AUSCULTATION[1]

Even an expert finds auscultation of the lungs much more difficult than auscultation of the heart, and to a beginner the former is especially difficult on account of many possible errors. First of all, there is the so-called *hair crepitation*, caused by the displacement of the hairs under the stethoscope with respiration. This occurs in persons with even a moderate growth of hair on the chest. The crepitations are synchronous with the respiratory movements, and an expert will quickly notice that the sound is just as marked during inspiration as during expiration, and that it is intensified by a careless use of the stethoscope. This source of error may be so annoying that it is necessary to wet the hair thoroughly with water, soap solution, or oil. If the hairs be too stiff for this procedure to be effective, the spot should be shaved.

Muscle sounds may also lead to error. In auscultating the apices the muscle sounds produced in the trapezius as it takes part in the respiratory excursion may be very disturbing. They may simulate rough breathing or even râles. It is important to be able to recognize this condition, so as to avoid error. Muscle sounds may also be produced by fibrillary contraction of muscles, *e. g.*, "shivering," due to the exposure of the examination. These sounds may be appreciated long before shivering is apparent to the eye. Such sounds may be differentiated from the respiratory murmur by asking the patient to hold his breath; if they persist, they are not respiratory. Besides these active muscle sounds there is a so-called "passive variety," which may be produced by the displacement of bundles of muscle-fibers under the edge of the stethoscope by light movements of the instrument or by the respiratory excursion of the chest itself. These sounds may be recognized by intentionally moving the stethoscope, and so reproducing them even when the patient is not breathing. Again, such sounds will not be heard when examining with the naked ear or when very gently applying the stethoscope. Other sounds originate from similar conditions, as, for instance, that produced by pressing the stethoscope over the lobulated fat in the female breast. These sounds frequently resemble crepitation very closely. They disappear when the stethoscope is used properly, and reappear when a little pressure is exerted, even when the patient stops breathing.

In auscultating portions of the body which are difficult of access a beginner is often liable to produce *typical friction sounds* artificially, especially if he be in an uncomfortable position, and if his stethoscope be not accurately or firmly applied, so that the patient's skin beneath it moves with respiration. Hence, it is a good plan for him to confirm his examination by listening with the naked ear or after carefully readjusting his stethoscope. If the skin be greasy or sweaty, it should be rubbed clean with a dry towel.

[1] This section appeared in the first edition of this work in 1894, long before Treupel's article on the same subject, and, therefore, is in no way based upon Treupel's work.

There are a great many other opportunities for producing extraneous sounds and so confusing the examiner. We might emphasize the necessity of persuading patients that their chests should be entirely uncovered for a proper examination, that they should not scratch themselves during the examination, and should remain absolutely quiet. It is perfectly useless to attempt an examination, particularly of the apices of the lungs, unless the patient's upper chest is entirely uncovered. A patient's false modesty, his fear of catching cold, or the examiner's laziness—none of these reasons can possibly excuse a careless examination.

It is desirable for every physician to accustom himself thoroughly to the use of one form of stethoscope. Even if he be accustomed to a poor instrument, he will make much better use of it than at his first attempts with a better one. Stethoscopes differ decidedly in their reproduction of consonation, *i. e.*, bronchial phenomena. The popular hard-rubber stethoscopes, for example, with comparatively long, open bells and thin, smooth walls, increase the resonation very decidedly. Mixed breathing through one of these instruments sounds much more bronchial than through a cylindric wooden stethoscope. Râles assume a more consonating character when heard through the former, a fact which the author considers a practical proof that consonating râles are produced by resonation and consonation.[1]

Another source of error in auscultating the chest may be mentioned. If the stethoscope bell be carelessly applied to the chest-wall, so that part of its edge does not rest there firmly, but is slightly elevated, thus allowing the air free entrance to, and exit from, the bell, the examiner will frequently hear a very good imitation of bronchial breathing. The sound is, of course, due to resonation. Probably the noise of the patient breathing through his mouth is transmitted and exaggerated by the open bell. It is quite similar to the sound we hear when we place a large sea-shell with its opening near the ear; when external sounds ordinarily unnoticeable are so much exaggerated by resonation that children frequently imagine they hear the roaring of the sea.

AUSCULTATION OF THE HEART

We almost always need a stethoscope to auscultate the heart properly, because, for the sake of diagnosis, we wish not only to appreciate the sounds, but also to localize them as accurately as possible. We often need to auscultate the heart, both in the recumbent and in the erect posture, and sometimes in other postures. Hence, it is a good routine to auscultate every patient's heart, both while he is lying down and while he is sitting or standing up. (See Mitral Insufficiency and Aortic Insufficiency.)

[1] [The use of the single-barrel stethoscope preferred by Prof. Sahli is not common among the profession in America. Undoubtedly, many of his reasons for this preference are well founded; but a good binaural stethoscope will transmit the sounds quite as plainly, always provided that the examiner is thoroughly accustomed to the resonation of his own instrument. So many different stethoscopes have been advised by different authorities that it seems unnecessary to recommend any special type.—Ed.]

NORMAL AUSCULTATION SIGNS OVER THE HEART

The only sounds we hear over a healthy individual's heart are the so-called "*heart tones.*" The word "*tone*" is not used here in strict acoustic sense, because the sounds heard are more properly *noises*, and only quite rarely possess a distinctly recognizable pitch. French authors call normal heart tones "bruits normaux"; but the Germans and the English have retained the term "tone" despite its acoustic inaccuracy, and have reserved the word "geräusche" (noises, murmurs) for certain pathologic sounds to be discussed later. (See p. 326 for the distinction between tones and murmurs.)

We normally hear two heart tones over the entire precordia, and with increased cardiac activity they may often be heard at some distance from the cardiac region. They follow each other with a definite rhythm. They can be imitated by pronouncing the syllables "lubb-dupp," or by tapping a closed book quite lightly with the tips of the fingers. A short pause exists between the first and the second tone, and a longer pause ensues before another first tone occurs. The first tone (the so-called systolic tone) is synchronous with the apex-beat as felt in the fifth intercostal space, *i. e.*, the beginning of systole. The second is synchronous with the beginning of diastole, and is therefore called the diastolic tone.

Physiologists have proved that each heart tone is made up of several factors, and that the reason why at any point of the heart we hear only two tones is because all cardiac tones are either systolic or diastolic; in other words, all systolic tones are massed together, and so are all diastolic tones. In reality, six different tones arise over the heart—four systolic and two diastolic.

The four systolic tones originate:

1. Over the left ventricle, at the mitral valve.
2. Over the right ventricle, at the tricuspid valve.
3. Over the beginning of the aorta.
4. Over the beginning of the pulmonary artery.

The two diastolic tones originate:

5. Over the aortic semilunar valves.
6. Over the pulmonary semilunar valves.

Hence, no diastolic tone originates over the auriculoventricular valves, *i. e.*, over the ventricles.

It has been clearly understood for years that the diastolic tones could be produced only by diastolic tension of the semilunar valves. The origin of the systolic tones has, however, baffled investigators for some time. Without going into the historic presentation of this question, the present theory, which has apparently stood the test of physiologic and clinical observation, will be briefly mentioned. The systolic tone, which is heard at the apex, originates, according to this theory, principally from the systolic tension of the auriculoventricular valves, which are closed at the end of diastole. This view is supported by clinical observations. In addition, experiments upon the bloodless heart have proved that the muscular sound of the heart muscle also takes part in the production of this systolic tone. The expression "muscular sound" should not be construed in the same way as when that term is applied to the skeletal muscles. The muscle sound of a skeletal muscle is one whose pitch depends directly upon the number of individual contractions,

which together produce the condition of tetanus. The contraction of the heart is, however, single and not tetanic; hence, its muscular sound is very different from the skeletal muscle sound. The muscular sound of the heart is in reality a vibratory phenomenon caused by the sudden systolic tension of the heart; in other words, a systolic tension tone, of exactly the same character as, and coincident in time with, the tension tones produced at the auriculoventricular valves and over the large arteries (aorta, pulmonary artery). This conception, therefore, means that all systolic tones of the heart are identical in character and are due to tension of its walls, including its valves. The systolic tones over the aorta and pulmonary artery are referable to the systolic tension of the still closed semilunar valves. They are produced by the sudden increase in intracardiac pressure at the beginning of the systole.

As there is no reason to separate the tension tone at the great vessels —in so far as it occurs during closure time—from the tones of the auriculoventricular valves and the heart-wall tone, the six tones given in the foregoing scheme can be well reduced to four, 1 and 3, and 2 and 4 being united under the names of left and right intracardiac tension tones.

The supposition that the systolic tones over the great vessels originate in a similar way to the first tones over the ventricles and auriculoventricular valves, and that they all are due to intracardiac tension during closure time, is supported by the fact that they are all coincident in time, provided the tones over the vessels are auscultated very close to the heart. Still, the older theory that the systolic tone of the vessels is produced by the sudden forcing of the blood into them during systole is, to a certain extent, justifiable in as far as a second component of the first tone can very often be detected over the vessels as the blood is entering them, *i. e.*, in the beginning of the expulsion time. (See p. 322.)

Clinically, it has been quite generally accepted that the systolic tones originate not only at the auriculoventricular valves and over the ventricles, but also at the great vessels (aorta and pulmonary artery). This opinion has been attacked upon physiologic grounds. Nevertheless, the author considers that the clinical view is unequivocally supported by cases of mitral and tricuspid insufficiency which furnish systolic tones over the auscultation area of the great vessels, while no such tones can be made out over the ventricles. Such cases are not very rare. These systolic tones may then depend upon the intracardiac tension tone of the closure time or upon "the expulsion tone" in the great vessels or upon both together. The last alone can be positively demonstrated by the exhibition of a reduplication of the tone.

In the interpretation of the pathologic changes of the systolic tones which originate over the ventricles, the clinician has thus far concerned himself almost exclusively with that part of the tone which originates in the valves. Hence systolic tones which are heard over the left ventricle are commonly called "mitral tones," those heard over the right ventricle, "tricuspid tones." The so-called *muscular tone* has thus far proved of little diagnostic significance because we cannot readily distinguish it from the proper valvular tones. Certain impurities in the first tone, usually referable to the auriculoventricular valves, may, however, be caused by the muscular tone on account of the irregularities in the systolic tension of the heart muscle (*e. g.*, in fibrinous myocarditis). Perhaps finer methods of examination may be devised, so that we may be able to utilize the muscular tones in the diagnosis of diseases of the heart muscle. (See p. 321.)

In order to make an exact diagnosis of the condition of the different chambers of the heart we should separate the elements of the tones and distinguish them individually, although the above-mentioned six tones of the heart are so intimately merged into a mixed systolic and a mixed diastolic tone that an inexperienced ear can only perceive the same tone over the entire heart.

The fact that the projections of the arterial openings and of the valves upon the chest-wall are at some distance from one another (Fig. 152) enables us, according to the spot auscultated, to appreciate at will sometimes one elementary tone of the heart better, sometimes another. We do not, however, best accomplish such an acoustic separation by auscultating each valve exactly at the point of its projection upon the chest-wall, for these points of projection are situated

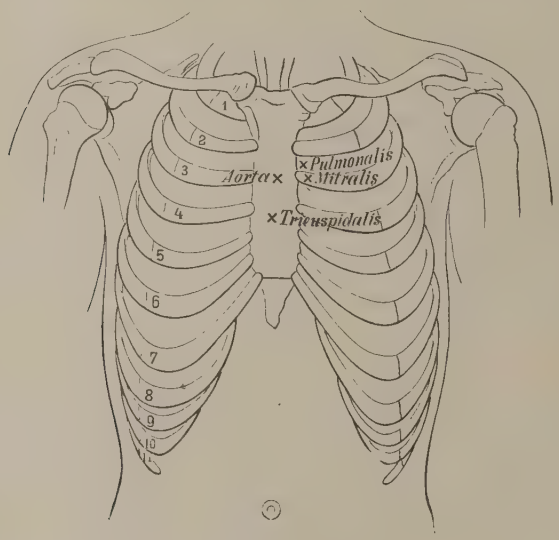


Fig. 152.—Projection of the heart valves.

rather near each other, as is shown in Fig. 152. Hence, the sounds at each point are quite confused. In practice, except for the pulmonary valve, which is auscultated exactly over its point of projection, we employ the following device: We set the stethoscope over the valve to be auscultated, and then move it away from this point of projection until we reach a spot where the tone we wish to auscultate can still be distinctly heard, but where the other tones, on account of their greater distance, are as faintly heard as possible and so no longer cause so much confusion. This device is founded upon the well-known law that the intensity of sound diminishes inversely with the square of the distance from its point of origin. By carefully noting the result of auscultation in valvular disease (including the substitution of murmurs for the tones of the affected valve) and by comparing such results with the changes subsequently found in the valves at autopsy, we are able to select

empirically the points at which each valve tone can be best auscultated separately.

The following relations between the sites of the valves (Luschka) and their respective auscultation points have been demonstrated by extensive experience:

The *mitral valve* is situated beneath the junction of the third left costal cartilage with the sternum; its *tone* is heard best over the apex-beat.

The *tricuspid valve* is situated halfway between the points where the left third and right fifth costal cartilages join the sternum. Its *tone* is heard best over the lower end of the sternum.

The *pulmonary valve* is situated in the second intercostal space, somewhat to the left of the edge of the sternum. Its *tone* is best heard at this point.

The *aortic valve* is situated about the middle of the sternum, at the level of the third costal cartilage. Its tone is best heard in the second right intercostal space, near the edge of the sternum.

The *mitral valve tone* is best heard at the apex, because the valve itself is overlapped by the lungs and by the right ventricle with the tricuspid valve, while at the apex the overlying lung tissue is very thin, and the left ventricle, in which the sound is produced, is not covered there by the right ventricle, or, at least, to a less degree than farther above. Further, the eccentric situation of the apex prevents the other heart tones from being so readily transmitted there.

The above statements explain why the rhythm of the heart tones differs at different points over the heart. The author will state the facts, and then attempt to explain them. Over the auscultation points for the aorta and pulmonary artery and in the vicinity, the heart tones exhibit an iambic rhythm (lubb-dúpp, lubb-dúpp).

Over the lower part of the sternum, however, and as far as the apex-beat, *i. e.*, over the auscultation points for the auriculoventricular valves (the ventricles), the heart tones produce a trochee (lúbb-dupp, lúbb-dupp).

This may be explained as follows: No diastolic tone is produced at the auscultation points for the auriculoventricular valves. The second tone is heard only by transmission from the aorta and pulmonary artery; consequently, it is proportionately diminished. Hence, the accent upon the first tone (trochée). The conditions are different over the great vessels, where both a first and a second tone are produced. Naturally, the first tone is relatively weak because it is produced by a moderate increase in pressure upon the roots of the great arteries acting against considerable arterial pressure at the beginning or closure time of systole. On the other hand, the second tone is much stronger and accentuated because it is produced by the rapid and forcible closure of the elastic semilunar valves acting under the pressure of the aorta and pulmonary arteries. This accounts for the iambic rhythm heard over the great vessels.

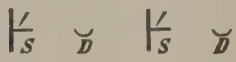
DISTINCTION BETWEEN SYSTOLE AND DIASTOLE IN AUSCULTATION

One of the most important requisites for the diagnosis of cardiac lesions is the ability to distinguish the systolic from the diastolic phase of the heart's action; in other words, to recognize accurately the systolic

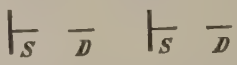
and diastolic tones. An experienced clinician does not find this especially difficult under normal conditions, because of the usual accentuation of the tones. The diastolic tone is accentuated over the great vessels, and the systolic tone is accentuated at the apex and over the tricuspid valve.

The sequence of the heart tones at the base of the heart and at the auscultation points for the auriculoventricular valves is shown by the following scheme (where the beginning of systole is indicated by a vertical line):

Great vessels:

Auriculoventricular valves: 

Some cases, however, furnish exceptions to the rule of accentuation in that the first and second sounds are more or less equally distinct. Under such circumstances the peculiarity of the pauses furnishes the most efficient means of differentiation. Both physiology and clinical experience have proved that systole is shorter than diastole; therefore the systolic tone is the one preceded by the longer interval of silence. In other words, if the heart tones be arranged in pairs, according to the interval of silence, and practice leads us to do this instinctively, the first tone of each pair will be the systolic, and the second tone the diastolic. In the following scheme of the heart tones the two heart tones are equally accented, but can be readily distinguished by the relative lengths of the pauses between them:



Even this method may be unavailable, because both the pauses are sometimes equal in length (pendulum rhythm). Then the clinician usually depends upon palpating the apex-beat. This is a practicable method provided the heart action be not too rapid and the apex-beat sufficiently forcible. If, however, the heart be too rapid, the time between the beginning of systole and diastole is too short to associate the sensation of touch with the perception of sound.

Comparing the heart tones with the carotid pulse is, when the heart action is rapid, even less reliable than comparing them with the apex-beat, as the apex-beat is synchronous with the first tone, while the carotid pulse corresponds more accurately to the expulsion time.

Systole can never be determined from the radial pulse unless the heart action be very slow. If rapid, the radial pulse is delayed (0.22 second, according to Landois), and so coincides more nearly with diastole than with systole. Students should, therefore, avoid this method.

Systole and diastole can, as a rule, be readily distinguished by one of these methods, but under certain pathologic conditions, where the heart action is very rapid, especially if it be irregular, the differentiation may be extremely difficult. Decision must be deferred in some cases until the heart action has quieted down, either spontaneously, by rest, or with the aid of drugs (digitalis).

In many heart lesions systole may be determined by certain well-

characterized pathologic heart murmurs, particularly those which are accentuated toward their termination and which occur only immediately before systole—that is, are presystolic. (See p. 334 et seq.)

In the above description the author has enumerated the different methods for recognizing the phases of the heart's action in the order of their practicability. The most desirable and the most commonly employed in practice is the determination of systole by the accentuation of the tones and their relation to the pause. Students should practise this method assiduously, and not form the habit of determining systole by feeling the carotid pulse, or, worse still, the radial pulse. The method recommended affords excellent practice in training the ear, and is of great importance to physicians who have never studied music.

THE GRAPHIC REGISTRATION OF THE HEART TONES AND THE CHRONOSCOPIC DETERMINATION OF THE LENGTH OF SYSTOLE

Hürthle, by means of the telephone, and Einthoven, by the string galvanometer, have both succeeded in registering the heart tones automatically. But in each method the apparatus is too complicated and expensive, and the procedure too tedious and difficult for clinical use. It is exceedingly desirable to obtain the same result by a simpler method, since the graphic registration of the heart tones is of the greatest clinical interest for the determination of the time of systole and diastole. Martius, so far as the author knows, was the first to employ auscultation for this purpose. By recording manually the results obtained by the sense of hearing, he has obtained important data for the interpretation of the normal cardiogram (see p. 365); but unless it has escaped the author, his method has not yet been adopted clinically. The author has experimented with this method with two purposes in view: (1) To obtain the means of interpreting irregular sphygmograms, since the registration of the heart tones gives the rate of the heart action (particularly important in the case of extra systoles); and (2) to determine the length of systole as an aid in the diagnosis of changes in the heart function.

In this case the point is the determination of the *interval* between the first and second heart tone, or the registration of *both* heart tones.

The author in general made use of the simplified Jaquet's sphygmocardiograph (see p. 126), recording the radial pulse directly, where this was demanded by the purposes of experiment, and simultaneously marking on the same paper, by means of the pneumatic writing apparatus, the heart tones as heard on auscultation. For this purpose the writing apparatus was connected with a rather thick-walled rubber tube, closed at the free end. This tube was struck by the finger, following the rhythm of the heart action. At each beat a mark was, therefore, made on the paper. The author used the rubber tube instead of the tambour, which Martius employed, because after the first stroke the drum membrane was likely not to come back into position in time for the second, in case the two tones were close together, so that a purely mechanical cause was apt to effect a delay in the registration of the second tone. Although this difficulty was obviated by the use of the rubber tube, another, already pointed out by Martius, remained the physiologic reaction time of the experimenter. The time required to appreciate the heart tone and to move the finger necessarily delayed the registration of the tone beyond its actual time. Martius showed that where the heart action is perfectly regular, this error is eliminated, since the ear of the experimenter becomes so accustomed to the rhythm that to a certain extent he gives the stroke at, and not after, the moment of the heart-beat. The author believes the correct explanation to be rather that the experimenter gradually comes to appreciate the length of time between the two beats and registers this interval rather than the exact moments of the beats themselves. For, from the moment when one grasps the length of the interval as an entity, it is no longer a question of the reaction time, but merely of the rhythm. But even then, as Martius has pointed out, results corresponding to those obtained by the *exact* marking of the tones are confined to cases where the heart action is absolutely and mathematically regular—and this is not the case, even under physiologic conditions. Strictly speaking, then, this procedure does not give an exact registration of the tones, especially in pathologic cases with irregular heart action. To be sure, it might possibly be conceivable that each experimenter after great experience, if he controlled his results by comparing them with the cardiogram, which, at least in

simple cases, gives directly the time of the second heart tone, might be able to determine his personal equation and make allowance for it in the curve. But these difficulties interfere only with registering the exact moment of the first heart tones.

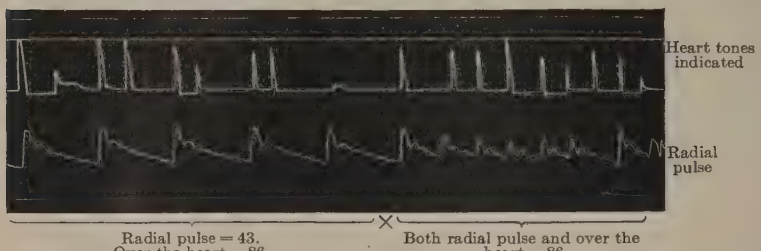


Fig. 153.—Pseudobradycardia caused by extra systoles.[1] In the beginning of the lower curve, apparent bradycardia. In reality, as shown by the succession of first heart tones, in the upper curve, it is a case of a regular sequence of extra systoles. In the second half of the lower curve the normal rhythm transpires until extra systoles recur. The apparent bradycardia is therefore a series of unshortened bigeminal pulses with compensatory pauses and wholly futile systoles.

They do not militate against correct results for either of the two purposes proposed above: (1) the determination of the rate of the heart action for the sake of the recognition of extra systoles, and (2) the determination of the duration of systole. In

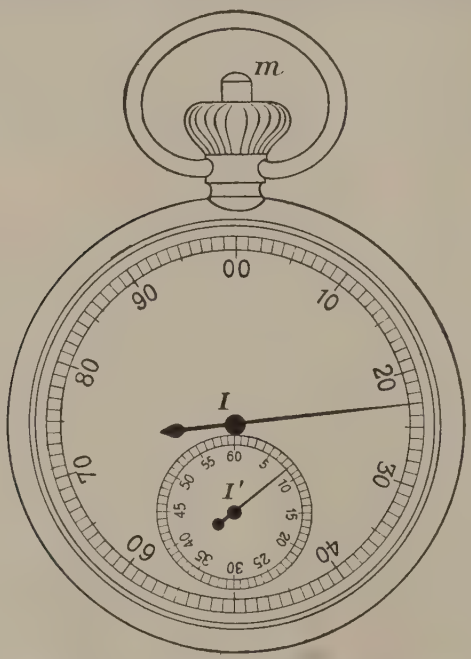


Fig. 154.—Pocket chronoscope (exact size).

the first case only the numerical registration, not the exact moment, of the systoles is required. (See results of such an experiment in Fig. 153.)

[1] This curve was registered by striking a drum instead of a rubber tube. The marks are too high for accuracy in marking the time.

In the second case—the determination of the duration of systole—the interval between the two tones is independent of the reaction time, since the latter delays equally the registration of each tone. The author, therefore, believes that valuable results concerning the length of systole may be obtained by this method, especially as by its means he has already determined that very considerable differences in this regard occur, *e. g.*, the prolonged time of systole in the so-called pendulum rhythm.

It is obvious that this method may be modified by discarding the graphic apparatus and simply registering the time of the beats on a watch held in the hand. For this purpose a stop-watch or chronoscope, giving fractions of a second, is necessary. Peyer, Favanger & Co. (Neuchâtel, Switzerland) have furnished the author with a suitable instrument.

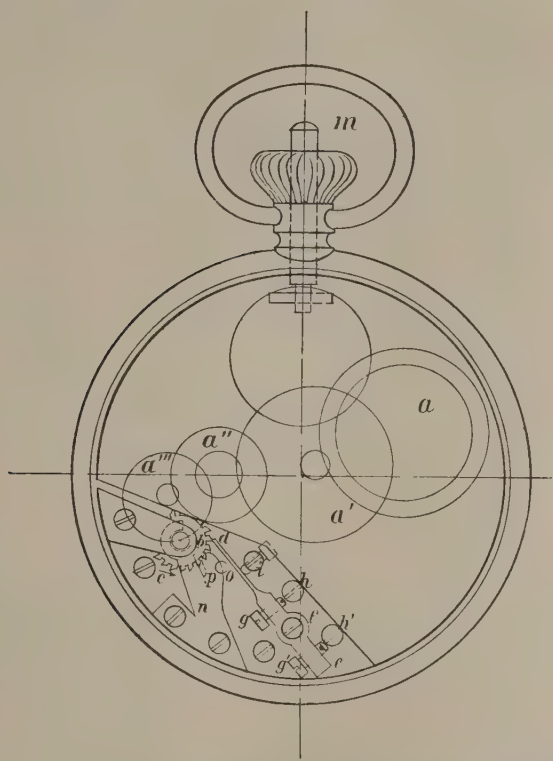


Fig. 155.—A part of the inner mechanism of the pocket chronoscope (exact size).

The large hand makes its circuit in one second; the small hand, in one minute. The time may, therefore, be read to $\frac{1}{100}$ of a second. Before using the watch, both hands must be brought to the 00 mark. By pressing at *m* the works are set in motion, as evidenced by the sound, but the hands do not move. At the beginning of the period of time to be measured the hands are set in motion by a second push at *m*, and at the end stopped in the same manner. After the time has been read off, a fourth push at *m* brings the hands back to 00. In order to secure the necessary uniformity of movement, the very delicate regulator of the Hipps chronoscope is used, instead of that of the ordinary watch.

An elastic steel tongue (*d*, Fig. 155), when struck, vibrates like a tuning-fork, thus producing the bugle-pitched humming sound heard when the works are set in motion. This engages with the brake wheel, *b*, and is set in vibration when the latter revolves. The rate of vibration of *d* governs the velocity of *b*, as, at each vibration of

the tongue, the wheel can revolve only through the distance of one tooth, *e. g.*, if *d* make 1000 vibrations a second and *b* has 20 teeth, *b* will revolve 50 times a second.

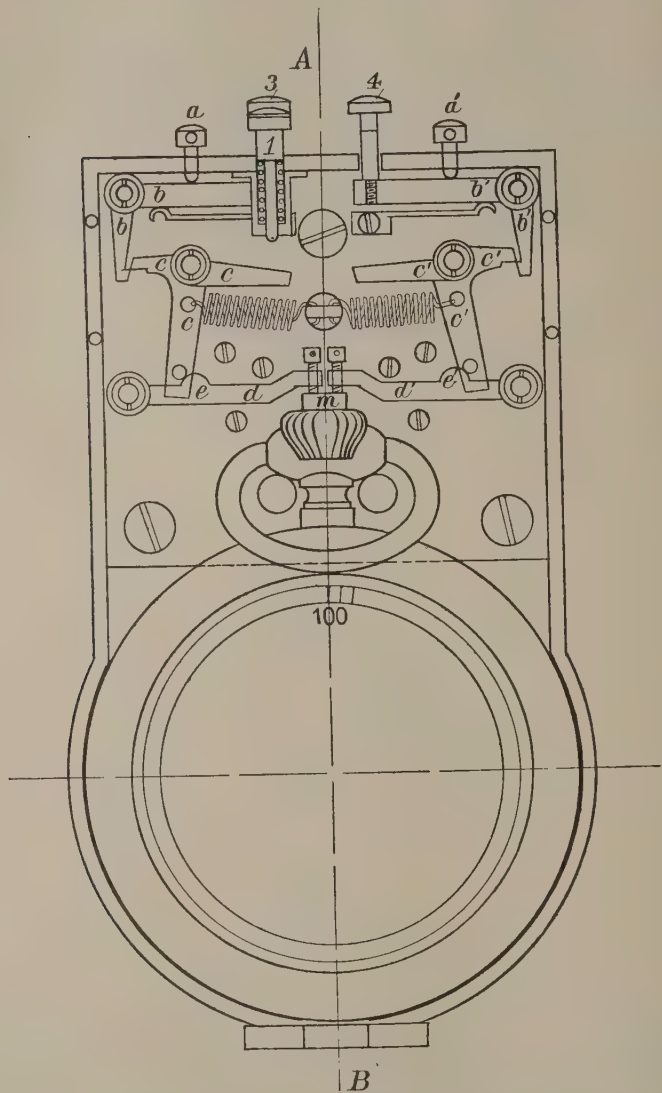


Fig. 156.—Pocket chronoscope in the case containing the mechanism for pressing *m*; the cover of the case removed; in the diagram the hands of the watch are omitted and the dial merely indicated (exact size).

The screw *i* serves to regulate the excursions of the steel tongue, and, therefore, the rate of vibration of *d*. *a* represents the spring casing, which is wound by the ordinary stem-winding mechanism. *a'*, *a''*, *a'''* represent the wheels, which accom-

plish the necessary transformation of velocity. a'' engages with b, which, therefore, governs the rapidity of the wheels, according to the rate of vibration of d. The axis of one of the wheels pierces the ground-plate of the watch in a direction perpendicular to the plane of the figure, and sets in motion the wheels that turn the hands. These are invisible in the diagram, being located on the other side of the ground-plate. The mechanism by means of which the four pushes at m accomplish the four results above described (setting the works in motion, setting the hands in motion, stopping the hands, bringing hands to 00 point) is not visible in Fig. 154, being situated on the other side of the ground-plate. It consists of an arrangement of levers similar to those of the ordinary stop-watch. Each pressure at m turns a swivel, which has four arms or sectors at right angles to each other, through a certain angle around its axis. The different positions thus occupied by the sectors correspond to the different positions of the levers. The first push, by displacing a spring, releases the brake wheel b, and so sets the works in motion. The second push inserts a movable connecting wheel between the moving works and the wheels that move the hands, thus immediately setting the latter in motion. The third push releases this connection and so stops the hands instantaneously, as their inertia is very slight. The fourth push, by means of an eccentric disc (the so-called "heart") brings the hands back to the 00 mark. The only part of this whole mechanism visible in Fig. 155 is the spring n, which sets free or arrests the wheel b as the spring p is shoved by the pin o. As the entire mechanism is of purely technical interest, it need not be described further here.

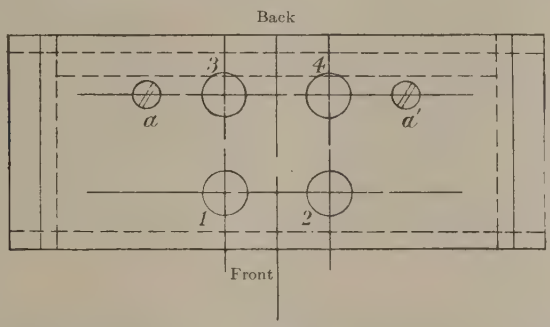


Fig. 157.—Diagram representing the top view of the apparatus, with the four buttons (exact size).

It is important for exact measurements that the works be set running before the time to be measured begins, in order that their initial inertia may have been overcome and they may be running at full speed before the hands are set in motion. The watch must always be fully wound and the observations be made only during the first three-quarters of a minute. After the small hand points to 45, the watch must be completely wound again and the hands set at 00. Otherwise, sufficient accuracy is not guaranteed.

When the time must be read accurately to within $\frac{1}{100}$ of a second, as in estimating the duration of systole, the time required to press at m causes a considerable error, so that the instrument must be modified by an arrangement to accomplish this automatically. Such an arrangement is shown in Fig. 116. By its means the finger of the experimenter, instead of completing the pressure at m, merely touches lightly the buttons 3 and 4 and the motion is completed by a previously stretched spring. The principle is similar to that of a hair trigger.

Fig. 156 shows the watch inserted in a nickel case. When the case is opened, the mechanism is visible and easily understood. As has been said, m must be pressed four times in measuring any given interval of time, as follows: (1) To bring the hands to 00; (2) to set the works in motion; (3) to start the hands; (4) to stop the hands. To accomplish these four ends, four buttons, 1, 2, 3, 4, are provided, as seen in the cross-section (Fig. 157).

In Fig. 157, 3 is shown behind 1; but on the other side, 2, in front of 4, is omitted. On the right side of the figure is shown the mechanism for the buttons 3 and 4; on the left, for 1 and 2. For movements (3) and (4) the very slightest possible pressure (50 gm. is sufficient) is necessary, in order that the error due to the time con-

sumed in the movement may be disregarded. For (1) and (2), on the contrary, the time taken is inconsequent and a strong pressure may, therefore, be utilized. This not only accomplishes the purposes already specified, but is also utilized for stretching springs *c* and *c*, thus setting the apparatus in the position needed for movements (3) and (4). Buttons 1 and 2 must, therefore, be pressed strongly; buttons 3 and 4 merely touched. Before the watch is placed in the case the hands must always be stopped. Fig. 156 corresponds to the moment when buttons 1 and 2 have been pressed. By pressing 1, the lever *c c c* has been set in the position shown. The left spiral spring has thereby been stretched, and the short arm *c* has engaged with *o*, thus leaving the apparatus ready for movement (3). The lever *b* has also pressed strongly on *m*, thus executing movement (1). After button 1 has been pressed it rises again by the action of the spring directly beneath it. Button 2, not shown in the figure, is then pressed, thus executing movement (2), and also stretching the right-hand spiral spring. The instrument is now ready for the actual measurement of a time interval. By a slight pressure on 3 or 4, *b* or *b′* is moved upward, *c* or *c′* released, the spring recoils, and the lever *d* or *d*¹ pushes *m* with such force and velocity that the loss of time in starting and arresting the hands may be neglected. The sensitiveness of the instrument is regulated by the screws *a* and *a′*, which change the degree of engagement between *b′* and *c′*.

Two buttons, 3 and 4, are provided rather than one, for starting and stopping the hands, not only for technical reasons of construction, but also in order that no time may be lost in lifting the finger, as would be the case if the same button and finger were employed for both movements.

ABNORMAL AUSCULTATION SIGNS OVER THE HEART

Only those abnormal results of auscultation, the determination of which is peculiar to auscultation, will be discussed here. Abnormalities in rhythm can usually be determined quite as readily from the pulse and the apex-beat, and will be discussed in the sections treating of the Pulse and the Apex-beat. The same sections describe the significance of the conditions under which the rhythm, as determined by auscultation and palpation of the apex-beat, differs from that obtained at the radial pulse. (See p. 152 and the section upon Reduplication of the Apex-beat.)

ALTERATIONS IN THE LOUDNESS OR INTENSITY OF THE HEART TONES

The intensity of the heart tones depends partly upon conditions within and partly upon conditions without the heart. The thicker the chest-walls, the less distinct the heart tones. Hence, in corpulent or muscular individuals, and particularly in women with well-developed breasts, the heart tones are apt to be faint, while in emaciated individuals they are generally loud. Edema of the chest-wall may also weaken the heart tones. Similarly, the heart tones are less audible if the heart be pushed away from the chest-wall, as a result of emphysema, of fluid in the pericardium, or of precordial emphysema. If a pericardial exudation be extensive, the heart tones are frequently quite inaudible.

They are intensified, however, if the lung be retracted from the heart as a result of pulmonary contraction or in consequence of an encroachment upon the intrathoracic space (kyphoscoliosis, high position of the diaphragm, or displacement of the heart).

The heart tones are intensified by a consolidation of the pulmonary edges about the heart. The factors operating here are probably the same as those which produce bronchial breathing over consolidations (p. 288 et seq.). The heart tones are more perfectly transmitted to the surface, on the one hand, through patent bronchi surrounded by consolidated lung, and, on the other hand, by resonance of the air in the bronchi. Resonance is also responsible for the intensification of the heart

tones in pneumopericardium and in adjoining cavities of the lungs, and also in certain degrees of distention of the stomach with air. In all these conditions the tones acquire a metallic ring.

In other cases, however, the heart tones are intensified or weakened on account of conditions within the heart itself. The intensity depends especially upon the strength of the heart. As a rule, therefore, the tones are louder in strong individuals or when the action of the heart is excited, while they are less audible or even inaudible in weak or very sick individuals, during collapse, and in serious affections of the heart muscle which diminish the capacity for work. Many exceptions to these rules occur in individual cases, because, as we have already seen, the intensity of the heart tones depends upon many other factors besides the mere strength of the heart. The elasticity and smoothness of the valves is one in point, and it may perhaps explain why the heart tones are occasionally very loud in weak individuals with low blood-pressure and in anemic persons. On the other hand, it is possible that a louder tone may be caused by increased rigidity of the valves. (See Increase of the Mitral Tone in Mitral Stenosis, p. 318 et seq.)

If the heart tones be increased, they may be audible not only over the precordia, but also at a greater or less distance from the heart, in the interscapular space, in the head, in the epigastric region, and occasionally even at some distance from the patient's body.

Increase or diminution of individual tones is of greater significance than uniform increase or diminution of all the heart tones. In order to recognize changes in the intensity of individual tones, we must clearly appreciate the relative intensity of the different heart tones under physiologic conditions. The corresponding tones of the right and left heart are generally conceded to be of equal intensity. This is true despite the greater power developed by the left ventricle, because the intensity of the tone depends not so much upon the absolute value of the pressure acting upon the valves, as upon the difference between the pressures acting upon the two sides of the valve at the moment of closure, and the rapidity of the increase in tension. Again, although the mitral and aortic tones of the left heart are naturally louder than the corresponding tones of the right heart, this difference in intensity is neutralized because the aortic and mitral valves are situated at a greater distance from the chest-wall than are the valves of the right heart. Even under normal conditions the corresponding tones of the right and left heart are, however, occasionally of unequal intensity; hence, an increase or diminution of one or the other tone cannot be considered pathologic unless the difference be very marked.

The second aortic tone is increased in hypertrophy of the left ventricle, provided the valves themselves are not seriously diseased and the hypertrophied ventricle is strong enough to produce an increase in blood-pressure. This occurs particularly in arteriosclerosis and in chronic nephritis. The second pulmonic tone is increased similarly in the hypertrophy of the right ventricle which accompanies mitral lesions, or in any other condition obstructing pulmonary circulation (emphysema). Accentuation of the second pulmonic tone is, therefore, an important sign of a compensated mitral lesion. Diminution or weakening of a second pulmonic tone which has been previously accentuated occurs when the compensation in these lesions becomes disturbed as soon as the right ventricle fails to exert sufficient power. But such accent-

uation is also often absent even without such failure of the ventricle, as may be easily understood from what has been said before and from consideration of the fact that the grade of valvular lesion also plays a part. Lüthje found that in healthy children of ten to fourteen years of age, the second pulmonic tone is regularly accentuated in comparison with the second aortic tone. He attributes this to the more important influence of the superficial position of the pulmonary artery at that age. [Creighton, working in Cabot's clinic,[1] showed "that in 90 per cent. of healthy children under ten years of age the pulmonic second sound is louder than the second aortic. In the next decade (from the tenth to the twentieth year) the pulmonic second sound is louder in two-thirds of the cases. About half of 207 cases between the ages of twenty and twenty-nine showed an accentuation of the pulmonic second, while after the thirtieth year the number of cases showing such accentuation became smaller with each decade, until after the sixth year we found an accentuation of the aortic second in 66 out of 68 cases examined."—Ed.] Under the above conditions, where the ventricle develops more force, we might expect that the *first* aortic and pulmonic tones, as well as those over the corresponding auriculoventricular valve, would be intensified. Although not usually the case, this is occasionally true. As has been mentioned above, the intensity of the first aortic and pulmonic sounds depends less upon the absolute pressure exerted by the ventricles at the beginning of systole than upon the difference in pressure on the two sides of the closed valve and the rapidity of the increase in tension. Similarly, the intensity of the auriculoventricular tones depends not so much upon the absolute force developed by the heart as upon the degree of systolic tension and the rapidity of its increase at the valve. Greater working power does not necessarily increase these two factors, provided sufficient blood enters the ventricle during diastole and at the same time places the valve under considerable tension.

Here must also be cited the frequently mentioned increase of the systolic tone at the mitral valve in mitral stenosis. The author believes that this is partly due to an acoustic deception arising from a peculiar accentuation of the tone, which abruptly interrupts the presystolic crescendo murmur. (See p. 335.) In other cases the abnormal loudness of the first tone may be due to the anatomic changes and the corresponding rigidity of the mitral valve. The same may be true of the tricuspid tone in tricuspid stenosis.

A diminution of individual heart tones is caused by more or less extensive destruction of the respective valves. Thus, marked deformity of the mitral valve causes diminution of the mitral tone, and marked destruction of the aortic valve causes diminution of the second aortic tone. At the same time, we must not forget that many erroneous views are held about this point. The loss of a portion of the membrane of a valve does not necessarily cause absence or even marked diminution of the corresponding tone, because the remaining portions of the valve can still produce the tones; and, besides, not only the valve itself, but also the surrounding structures, contribute to the production of tones. For the first tone the walls of the ventricle and the conus arteriosus, and for the second the walls of the first portion of the aorta and pulmonary artery, play an important part.

[1] Loc. cit., p. 176.

If a valve be affected, we shall hear not only the murmur the lesion causes, but also the normal tone. An experienced clinician can frequently detect both the murmur and the heart tone. This is best accomplished by holding the ear at a little distance from the stethoscope, so that the sounds are heard rather faintly. The respective tones may then be diminished by a valvular lesion, but are not necessarily so. It has been frequently stated that the diagnosis of aortic insufficiency depends upon an absence of the second aortic tone. This view is absolutely incorrect. A practised ear can hear the second aortic tone in most cases of aortic insufficiency, although it is often diminished. Absence or marked diminution of the second aortic tone may, however, aid in some cases in the diagnosis of aortic insufficiency.

It is interesting and quite important diagnostically to remember that with a marked insufficiency of the auriculoventricular valve, not only the auriculoventricular tone, but all the tones of that side of the heart, become very much diminished or disappear entirely. The absence of the first tone is not due to the impossibility of producing a first tone in an extensive destruction of the valve, for, as was noted above, the systolic tone originates in all that part of the heart put into a state of tension during systole, including the walls of the ventricle and the arterial openings. For example, a marked mitral insufficiency may show no systolic tone at any point over the left heart, and not merely the first, but also the second, tone over the aortic area may be entirely absent. The cause of this peculiarity is at first glance rather difficult to understand, but it may be explained as follows: On account of the existence of mitral insufficiency, the closure time of the heart disappears. Its place is usurped by a period during which the heart does contract about its contents, but the rapidity of increase of tension is very slow, because the blood in the ventricle immediately escapes into the auricle. Consequently, the mitral valve is never brought into a state of rapid and strong tension, because, as soon as the blood escapes into the auricle, both sides of the valve are subjected to about the same degree of pressure. Hence, the mitral tone is very faint or entirely lacking on account of the absence of a closure period. A further result of the regurgitation at the beginning of systole is that the walls of the ventricles, the conus arteriosus, and the closed aortic valves are not sufficiently nor suddenly enough stretched to produce a strong systolic tone. Consequently, either no systolic intracardial tension tone or only a rudimentary one originates over the ventricle and over the beginning of the aorta. In addition, a marked mitral regurgitation may also cause diminution or absence of the second aortic tone, because the blood regurgitated into the auricle by the ventricular pressure rushes back again into the ventricle at the beginning of diastole, thus reducing below the normal the difference in pressure upon the two sides of the valves, and their tension. Other things being equal, the same reasoning applies to the right heart and to tricuspid insufficiency. All the heart tones may be diminished or entirely absent in a combined mitral and tricuspid insufficiency. The absence of the heart tones in insufficiency of the auriculoventricular valves is of double diagnostic significance. In the first place, it aids in determining the degree of insufficiency. Mitral insufficiency with no tone over the left heart must necessarily be a serious lesion. This law applies only during the period of compensation. During disturbance of compensation the heart tones may be enfeebled

on account of diminished systolic force. On the other hand, the absence of heart tones may occasionally prove the existence of an auriculoventricular insufficiency which could not otherwise be diagnosed on account of the absence of a mitral murmur. If, for example, a compensated mitral stenosis be diagnosed, and it be noted that the heart tones are absent on the left side, the stenosis is probably combined with an insufficiency of the mitral valve.

Finally, in regard to the audibility of heart tones in valvular lesions accompanied by murmurs (see p. 327), it is to be noted that the statement so frequently made, that the tones are masked by a murmur, is based on an erroneous conception. The same change which disturbs the functions of the valves and produces the murmur may coincidentally prevent the production of a tone or diminish its force. The tones cannot, however, be masked by the murmur. Provided the tone actually exists, its sound, like a sharp blow in the midst of the slow, pulsating sound of the murmur, can always be detected by an experienced clinician, especially if he employ the device of holding the ear at a little distance from the stethoscope. (See p. 318.)

In the graphic representations of the results of auscultation the author has expressed the intensity of the heart tones by the heaviness of the metric signs and accents used to represent them. (See, for example, Fig. 173, the diagram of mitral insufficiency with increased second pulmonic tone.)

ALTERATIONS IN THE TIMBRE OF THE HEART TONES

The timbre or quality of the heart tone may vary even under normal conditions. Whether the normal heart tones are simply noises or whether they resemble musical tones depends upon a number of factors difficult to analyze, especially upon the elasticity of the valves and of the walls of the larger vessels. However, a drum-like or ringing quality is rather rare in healthy individuals. Occasionally the tones, even in healthy individuals, are not clear; they are not like a single short blow, but produce a rough, irregular sound. The cause of such an impurity in the tones of a normal heart has not been fully determined; but apparently indistinct reduplication of the tones (see p. 321) and rudimentary murmurs which occur even in the normal heart are the chief factors.

Marked variation in the timbre of the heart tones occurs under pathologic conditions. Thus, in arteriosclerosis the second aortic sound is not only accentuated, but possesses a peculiar ringing quality. Moreover, as has been mentioned upon pp. 316 and 317, as a result of resonance of air contained in cavities, the heart tones are not only intensified, but assume a peculiar metallic character.

The tone called "cliquetis metallique" is a noticeably rattling systolic tone heard over the ventricles when the heart action is stimulated, not only in healthy individuals, but also in heart disease, in attacks of nervous palpitation, and in every form of cardiac hypertrophy. Occasionally it can be heard at some little distance, and is probably due to the violent vibration transmitted to the chest-wall, or possibly the stomach, in consequence of the accelerated cardiac action.

Impurity or roughness of the heart sound is observed in healthy persons, but it is more commonly due to some disease of the heart. It is frequently due to slight changes in the valve which do not necessarily

disturb its function, merely affecting its uniform tension (roughness or rigidity of the curtains, pathologic deposits on the valve cusps), but in some cases it is the result of a valvular lesion which is not sufficiently pronounced to produce the characteristic murmur. Under such circumstances an impure tone might be regarded as a rudimentary murmur; because, if the cardiac action be accelerated, *e. g.*, by directing the patient to get up and to sit down again several times in succession, the impure tone is frequently replaced by a true murmur. Autopsy findings occasionally suggest that the impurity of the systolic tone is due to changes in the muscle sound, the result of structural changes in the heart muscle (fibrosis).

APPARENT OR ACTUAL REDUPLICATION OF THE HEART TONES

Normally, only two tones are heard over every point of the heart, a systolic and a diastolic tone; but under both physiologic and pathologic conditions three or even four tones may be distinguished. This peculiarity may depend upon either one of two causes: either there is only an apparent reduplication, *i. e.*, under normal conditions all systolic tones and all diastolic tones occur at the same moment, but in any given case such a coincidence may be disturbed, or else there may be an actual reduplication of the sounds, due to the production of abnormal tones.

Division, Splitting, and Reduplication of Heart Sounds ($\frac{2}{4}$ time).—When two tones with a very short interval between them are heard in place of one heart tone, the tone is said to be split or reduplicated. If the two tones occur very close together, we speak of a *division* or *splitting* of that heart tone, while we limit the term *reduplication* to those cases where the two tones are separated by a longer interval. The three tones do not follow each other in $\frac{3}{4}$ time, but the heart rhythm preserves the normal $\frac{2}{4}$ time. Reduplication of the first sound gives an anapest, ⏑ ⏑ — (lubb-lubb-dúpp); reduplication of the second sound, a dactyl, — ⏑ ⏑ (lúbb-dupp-dupp).[1] The double tones in splitting, which is only indistinctly separated from reduplication, are repeated so rapidly that the examiner obtains the impression of a single tone accented at the beginning or at the end. This is commonly expressed by combining the metric signs ⏑⏑ and ⏑⏑.

This splitting or reduplication may be caused—(*a*) by an imperfect coincidence of the normally synchronous tones of the right and left heart, or (*b*) by the production of abnormal tones.

(*a*) **Splitting and Reduplication as a Result of Imperfect Coincidence of the Normally Confluent Heart Tones.**—It is not surprising that various conditions should disturb the coincidence of the heart tones, considering the great number of factors influencing the course of the heart's action (nervous influences, variations in pressure in the different parts of the heart chambers and in the rest of the circulation). It is, on the contrary, more remarkable that any such coincidence of all systolic and all diastolic phenomena should occur at all; and suggests a very perfect balance of the cardiac mechanism.

[1] The normal accentuation of the systolic tone over the auriculoventricular valves and of the diastolic tone over the great vessels is effaced by the splitting of the tones. Hence, reduplication and splitting of the first tone produces an anapestic rhythm, not only over the great vessels, but also over the auriculoventricular valves. In the same way splitting of the second tone produces a dactyl, not only over the auriculoventricular valves, but also over the great vessels.

In cases in which this coincidence is lacking, the splitting and reduplication may be heard best half way between the corresponding valve areas of the left and the right heart.

Faulty coincidence, producing a reduplication or splitting of the first tone, is occasionally caused by a failure of the two ventricles to contract at the same moment; under such circumstances the splitting of the tone must be audible over the entire heart.

In many other cases the reduplication or splitting of the first tone, which is heard only over the great vessels, might readily be assumed to consist of the normal first tone, which is increased by the tension of the closed semilunar valves, plus a second part of the tone, which is produced during the expulsion time by the pulse-wave in the aortic or pulmonary artery. As a matter of fact, there is no reason why the pulse-wave which can produce a tone in the carotid artery should not produce such a tone in the aorta. Such a splitting of tone does not occur normally, because the closure time is so short that the tone of closure time and that of the expulsion time are merged into one. Accordingly, the reduplication or splitting of the first tone, as heard only over the great vessels, would depend upon a prolongation of the closure time, and thus possess some clinical significance. This explanation agrees with the physiologic reduplication of the first tone, heard over the great vessels, particularly during those phases of respiration where arterial pressure is elevated (according to p. 135); that is, with slow respiration, during inspiration, with rapid respiration during expiration.

In a recent article,[1] R. Geigel maintains that this kind of reduplication, depending upon an expulsion tone in the aorta and pulmonary arteries, audible apart from the intracardial tension tone, may regularly be heard under normal conditions if one listen to the whole heart projection, instead of confining one's self to the classic spot for auscultating the great vessels. As the author has already pointed out, there is no doubt that the blood, streaming into the aorta, produces as distinct a tone in it as in the carotid. Moreover, there is very frequently time for this tone to be appreciated by the ear as separate from the intracardial tension tone, since the closure time is about 0.07 second, and according to Helmholtz (cited by R. Geigel), the ear can appreciate two short sounds 0.01 second apart. R. Geigel attributes the neglect of this phenomenon to its lack of diagnostic applicability. For its demonstration one must, according to Geigel, listen from the apex toward the great vessels. An intermediate territory will always be found where the splitting is to be heard. From this spot the first tone becomes the more prominent—and finally the only one—toward the apex; the second, toward the vessels. It is seldom a question of a distinct reduplication, but rather of a splitting or even only of an impure first tone.

Faulty coincidence, producing a splitting of the second tone, is frequently observed in healthy individuals in the beginning or during the course of inspiration and in mitral lesions—both insufficiency and stenosis. A common explanation of the splitting of the second tone is that the aortic and pulmonary semilunar valves do not shut at the same instant. This lack of coincidence, under the above-named conditions, is supposed to be due to an abnormal difference in pressure between the aorta and pulmonary artery. High pressure closes the valves sooner than low pressure. The second part of this explanation

[1] Münch. med. Woch., 1906, No. 17.

is certainly incorrect, because even under physiologic conditions the pressure in the aorta differs enormously from that in the pulmonary artery, and because, furthermore, Ceradini has demonstrated that the closure of the semilunar valves occurs instantly and independently of the degree of pressure in the artery as soon as blood ceases to flow out of the heart. The second tone is not caused by the closure, but by the sudden tension of the closed semilunar valves, and takes place at the moment when, after a period of rest, the ventricular diastole begins. So far as any lack of coincidence of the left and right tones is concerned, splitting or reduplication of the second tone might be referred to lack of coincidence in the beginning of diastole, but such an assumption is quite unnecessary. The following explanation is more plausible: The semilunar valves, which are closed at the end of systole as a result of the marked diastolic drop in pressure within the ventricles, are suddenly forced back and made tense against the ventricle by the pressure in the aorta and pulmonary artery at the beginning of systole. This produces the diastolic tone. Any factor which tends to prevent a rapid diastolic drop in pressure within the ventricles will probably delay the corresponding second tones, while any factor which favors a drop in pressure will hasten it. As a matter of fact, such factors are present under those conditions where reduplication or splitting of the second sound exists.

Inspiration in a healthy individual, with moderately rapid respiration (see p. 134), detains the blood in the dilated pulmonary vessels, and so delays the filling of the left ventricle. As a consequence, the difference in pressure between the aorta and the left ventricle is rapidly increased, producing sudden diastolic tension of the aortic valves, and thus causing the second aortic tone to occur before the second pulmonic, as evidenced by reduplication or splitting of the second tone. The conditions are similar in mitral stenosis, where the flow of blood into the left ventricle is obstructed by the narrowed valve; consequently, the aortic valve is put under tension sooner than the pulmonic. In mitral insufficiency, on the contrary, the left ventricle is filled very rapidly during diastole, on account of the congestion in the auricle; consequently the aortic valve is put under tension somewhat later and the second aortic tone is delayed. If this explanation be correct, the second aortic tone is hastened during inspiration of a healthy individual, as well as in mitral stenosis, but delayed in cases of mitral insufficiency. This is actually the fact, because in mitral stenosis and in healthy individuals the second part of the double tone can be perceived in the left intercostal space as a loud second pulmonic tone, while in mitral insufficiency in the same place, the first part of the double tone is more distinctly heard.[1]

Reduplication of the second tone so frequently accompanies mitral lesions that it should be considered as of some diagnostic significance, provided that it can be proved to be independent of any definite phase in breathing.

(*b*) **Splitting and Reduplication as a Result of the Production of New Tones.**—In some cases the reduplication of tones is due not to

[1] [To prove that this explanation is correct, we should determine whether the inspiratory can be changed to an expiratory reduplication in healthy individuals breathing very slowly; because slow respiration produces exactly an opposite effect upon the ventricular filling from rapid respiration.—Ed.]

failure of coincidence of the normal tones, but to the production of new abnormal tones. The splitting and reduplication are then heard most distinctly at a particular valve area, not midway between two. Gallop rhythm is an exception, being often heard over the whole heart. (See p. 325.)

Splitting or *reduplication of the first tone* over the auriculoventricular valves may occur where mechanical conditions, *e. g.*, considerable differences in size of the individual valve segments, prevent them from being put under tension at exactly the same moment, so that they produce separate systolic tones.

This explanation would even account for the occurrence of a triple tone at the tricuspid valve.

In certain cases the *reduplication* or *splitting of the second tone* is also due to the production of new tones and not merely to lack of coincidence. Circumstances are conceivable where marked secondary elevations (dicrotism) due to elasticity or reflected waves of the aortic pulse may cause a supernumerary second tone. Furthermore, a new diastolic mitral tone may produce the rhythm of reduplication instead of a triple rhythm. (See p. 325.)

Triple Rhythm ($\frac{3}{4}$ **Measure**).—1. *The triple rhythm of the heart tones in mitral stenosis* consists of three approximately equal tones, heard either exclusively or most plainly at the apex and over the mitral area. There is no such grouping of two of the three tones, described above as reduplication (splitting or doubling), but the heart, instead of beating as normally, in $\frac{2}{4}$, beats in $\frac{3}{4}$, time. The accent ordinarily falls upon the second of the three tones.[1] With this rhythm the typical murmur of mitral stenosis (see p. 334) may or may not be audible. If inaudible, it may be brought out by simply accelerating the cardiac action, and we then find that a presystolic murmur usurps the place of the first of the three tones, thus proving that the latter is an abnormal presystolic tone. The second is the normal systolic tone, and corresponds to the apex-beat; and the third is consequently the diastolic tone. The localization of the extra tone (the first stroke of the triple rhythm) at the auscultation area of the mitral valve is another argument for its origin from this valve. It is, therefore, an abnormal presystolic tone. The thickened cusps of the mitral valve remain tense during ventricular diastole, and so the auricular contraction plus the valvular tension produces the tone. The adherent mitral valve in this case forms a diaphragm between the auricle and the ventricle during diastole; and just as the systolic vibration of this diaphragm occasions a systolic tone, so does a presystolic (diastolic) tension from the auricular contraction occasion a new presystolic tone. This sort of triple rhythm is readily appreciated in typical cases by the presystolic character of the first tone; and it is of diagnostic importance in recognizing cases of mitral stenosis not accompanied by a presystolic murmur. (See p. 321.) One should, however, be careful not to confuse triple rhythm with another very common peculiarity of mitral lesions, viz., reduplication of the second tone, due to the imperfect coincidence of the second aortic and second pulmonic. The rhythm in this case is quite different and the localization over the mitral valve is especially characteristic of the presystolic tone. (See p. 321.)

[1] At the mitral area } ◡ ◟ ◡ ◡ ◟ ◡ { tatáta tatáta
at the apex. } lubblúb-dupp lubblúbdupp.

It must, however, be stated that the diastolic mitral valve tone of mitral stenosis is not always presystolic, for it may appear at another period of diastole, in case tension of the mitral valve occurs not only during the presystolic contraction of the auricle, but also at any earlier period of diastole, from the recoil of the blood at the adherent mitral valve. In such cases exactly the same rhythm results as in reduplication of the second tone (p. 321 et seq.); and the significance then can be determined only by its appearance over the mitral valve, as contrasted with its ordinary appearance over the base or at the apex.

2. *Gallop rhythm* is a triple rhythm, heard, for the most part, over the entire heart; the tones follow at approximately equal intervals, and the second ordinarily is accentuated at the apex and the third at the great vessels; thus:

Apex: ◡ ◜ ◡ ◡ ◜ ◡ tatáta tatáta
Great vessels: ◡ ◡ ◜ ◡ ◡ ◜ tatatá tatatá

This rhythm means that an extra tone occurs during diastole, *i. e.*, before the normal first tone. We can ordinarily distinguish it from the presystolic tone of mitral stenosis, because it is generally to be heard with nearly equal distinctness all over the heart.

Its explanation is not yet quite certain. We have no physiologic grounds for supposing that the contraction of the ventricle takes place in two steps. Potain[1] formerly held that the auricular contraction made the ventricular wall tense and so produced the first of the three tones; and Kriege and Schmall's[2] cardiographic representations supported his theory. Potain, however, later[3] modified his explanation, to the effect that the extra tone which occurs during diastole, or before systole, is not due entirely to the contraction of the auricle making the heart-walls tense, but also to a sudden, abnormal passive tension of the ventricular wall during diastole, which tension is occasioned, in the first place, by the *vis à tergo* of the entering blood, and, in the second place, by the auricular contraction. The extra tone frequently coincides with presystole; but sometimes it approaches more nearly the preceding diastolic tone than the following systolic tone, and so makes the rhythm quite different. In addition to the normal systolic shock we can frequently feel or see a diastolic or presystolic shock of the anterior heart-wall, coinciding with the extra tone, so that the above explanation seems quite probable.

Such an explanation makes *gallop rhythm* the expression of an abnormally stimulated heart activity, which produces either an abnormally quick diastolic relaxation and a consecutive sudden passive tension of the ventricular wall from the entering blood, or an increased contraction of the auricle.[4] Conditions which apparently are directly opposed, produce a gallop rhythm, viz., *cardiac insufficiency*, which is always connected with an irritability of the heart; and the *stimulated*

[1] Union med., November 11 and 18, 1876; January 6 and 27; February 29, March 11, 1875.

[2] Zeit. f. klin. Med., vol. xviii, 1891, parts 3 and 4. [3] Sem. méd., 1900, p. 22.

[4] Stefani's experiments concerning the effects of digitalis on diastole in artificial pericardial effusion give some support to the view that diastole of the ventricle is an active process. In that case a stronger ventricular diastole may be the cause of gallop rhythm. Brauer (Cong. f. inn. Med., 1904) inclines toward this view, especially since his graphic demonstration of the force of his so-called "thoracic rebound." Sherrington has shown that relaxation of the external rectus muscle of the eye may protrude the eyeball, which is the direct opposite of its contraction, so that assuming an active ventricular diastole is not so unreasonable as might appear at first sight.

cardiac action of *health*, of *exophthalmic goiter*, and of *nephritis with high-tension pulse*. Potain distinguished between a gallop of the right and of the left heart, according to whether the rhythm is heard more plainly over the right or the left side.

Gallop rhythm, then, is a diastolic phenomenon. Potain's "*systolic gallop rhythm*" is better called a doubling of the first tone (p. 322). It is heard over the great arteries, and is due to a prolongation of the closure time.

PENDULUM OR FETAL RHYTHM OF THE HEART TONES
(Embryocardia)

By this is understood a rhythm in which the pauses between the systolic and diastolic equal those between the diastolic and the systolic tones, *i. e.*, the short and the long pauses are equalized. Pendulum rhythm has been principally observed with increased tension in the arterial system (*nephritis*). Pawinski's [1] experiments seem to prove that it depends upon a prolongation of the systole, and essentially of its closure time, which, in turn, is due to the increased arterial pressure the ventricle has to overcome before it can open the semilunar valves.

Huchard designated as *embryocardia* a characteristic form of cardiac action observed in severe infectious conditions and in the terminal stages of heart disease. On account of the great rapidity of cardiac action both pauses appear to have almost the same duration and both tones the same resonating character. Embryocardia should therefore be defined as tachycardia plus pendulum rhythm. Stokes described the same phenomenon some time ago under the name of fetal-heart tones. Its explanation is still unknown.

HEART MURMURS

These are variable sounds heard either in addition to the tones or sometimes usurping their place. They are nearly always due to some diseased condition, but they are occasionally heard in health.

An exact distinction between *tone* and *murmur* is not essential here. Acoustically, the heart tones depend as much as the murmurs upon non-periodic sound vibrations, so that it is not correct to describe tones as consisting of regular, and murmurs of irregular, sound vibrations. An approximate periodicity or regularity of the vibrations in these sounds, and thereby an approach to a definite pitch, is doubtless far more applicable to murmurs than to tones, *e. g.*, many murmurs are best described as musical. For practical diagnosis the distinction between *tone* and *murmur* depends chiefly upon the kind of dissonance, and this, of course, upon the method of origin. The *tones* of the heart arise from a single sudden disturbance of equilibrium of the sound-producing body; the *murmurs*, on the contrary, from several repeated disturbances of equilibrium. Any evident duration in the *tone* must depend upon continued vibrations of the part due to its inertia; in the *murmur*, on the contrary, upon repeated fresh vibrations due to new applications of the moving force. Thus a tone may be compared to the sound produced by striking once upon a drum; and a murmur, to the sound produced as long as one blows in a pipe. Acoustically, they are noises in either case, though they may approach more or less nearly to a musical tone or resonance. Tones, then, can be distinguished from murmurs essentially by their brevity and by the rapid, almost instantaneous, dissonance. What has been mentoned

[1] Deut. med. Woch., 1891, No. 4.

above in regard to murmurs and tones of the heart is quite as true in regard to those of the vessels. (See p. 347.)

Some of the murmurs heard over the heart originate from within, some from without; the former are called *endocardial*, the latter, *pericardial*.

Endocardial Murmurs

These are of two kinds: *valvular murmurs*, depending upon a disturbance of the cardiac valves, and *accidental murmurs*, having no connection with a disturbed valve function.

Endocardial murmurs are more or less prolonged noises (thus contrasting with the heart tones, which are brief and sound sharply cut). They are very diverse in character, generally blowing or puffing, sometimes scraping, musical, even singing or whistling. The heart tones are expressed symbolically by the metric signs and ⌒ ⌣ and the endocardial murmurs by the crescendo and diminuendo signs < and . Two elementary forms of murmurs may be differentiated:

1. > Diminuendo murmurs, which begin sharply and gradually fade away.
2. < Crescendo murmurs, which begin gradually and end sharply.

Two combined forms may be derived, thus:

3. ◇ Murmurs which begin, and fade away, gradually.
4. ✕ Murmurs which begin and end sharply, and which in the middle are of minimum intensity.

In most cases the *endocardial murmurs* are audible only to auscultation; but exceptionally they may be heard at a distance, or even appreciated by the patient himself. These so-called distance murmurs have generally a musical, singing, or whistling character.

We are indebted to the experiments and researches of Corrigan, Kiwisch, Heynsius, Thomas, Weber, Chauveau, Marey, Thann, Nolet, and others[1] for the physical explanation of the peculiarities of endocardial murmurs such as those mentioned above. Normally, the blood flows through the heart chambers without noise, so that a murmur must be attributed to some abnormality of the blood-current in the heart, as the following experiment illustrates:

If we have a glass tube (*a b* in Fig. 158, I) through which a stream of water is flowing, no murmur can be heard at the point *c* so long as the current is moderate. If, now, the rapidity of the current be increased by supplying more water, a continuous blowing sound can be appreciated at *c*, which simulates to a certain extent an endocardial murmur. Such a simple experiment explains the *first essential* for the origin of endocardial murmurs, namely, *the rapidity of the current*, which, other conditions remaining the same, naturally depends upon the hydraulic pressure causing the stream.

By narrowing or widening the caliber of the tube at a certain place (*c* in Fig. 158, II, III, and IV) we possess another means of producing a murmur in the silent current, always provided the rapidity of the stream is sufficient. If in such a tube the murmur be not heard, it may be produced, or if very faint, it may be intensified by increasing the rapidity of the flow, although the same rapidity in the straight tube

[1] An excellent historic presentation of our knowledge of heart murmurs is found in Rosenstein's section on Heart Diseases, in Ziemssen's Handbuch der spec. Pathol. u. Therapie, vol. vi.

would furnish no sound. This, then, explains the *second essential* in the formation of endocardial murmurs, viz., *alterations in the caliber of the blood-channel.*

In order to clear up these fundamental principles let us assume, as is pictured in Fig. 158, III, that the fluid flows from a narrower into a wider part of the tube. Experimental physics teaches us that under such circumstances the fluid exerts a certain suction power upon its surroundings. This, in our supposed case, to a certain extent narrows the widened portion of the more or less elastic tube. Hence the difference in the lumen is lessened; the suction ceases, the walls of the tube bulge again, and the process is repeated over and over again as long as the current flows. Thus the current occasions lateral vibrations of the widened part of the tube-wall; and, secondarily, of the narrower part, which alternate with those of the widened part and follow the same rhythm. Thomas Weber claims that the murmurs arise from these vibrations of the tube-wall, and that they are transmitted just as well against as with the stream. If the narrowing be sharply localized, as in Fig. 158, II, the result is the same. And even as in Fig. 158, IV, where a widened tube is suddenly and permanently narrowed, the origin of the vibrations of the wall are exactly the same, whether the current is in the direction of the lower

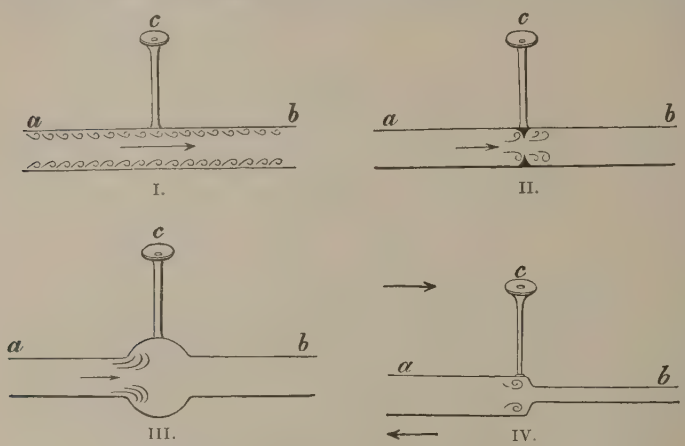


Fig. 158.—The origin of current murmurs: *a*, *b*, Current of water; *c*, stethoscope.

or of the upper arrow. In the former, suction takes place as in III. In the latter, the fluid streams from the wide into the narrow tube, and the action of the pressure occasioned by the narrowing is like that of the suction in III. It is easily understood that a sufficiently rapid current will produce murmurs even in tubes of uniform caliber, as in I. For friction is always to be found in the external layers of streams, and so the layers quiescent against the wall rubbed upon by the more active middle, current layers, act like an infinite number of microscopic stenoses. Weber has proved in these experiments that the murmurs over the wider part of the tube always appear stronger than over the narrow. And this is easily understood when we remember that, according to Pascal's law (the law of the hydraulic press), the vibrations in the wall causing the sound increase in proportion to the size of the contact surface between fluid and wall. This is of great importance in the explanation of the relations of transmission of the cardiac murmurs. It can be demonstrated experimentally only upon rubber tubes, since stiff tubes (of glass or metal) transmit the sound too perfectly and too far.

The following experimental facts, adduced by Weber, are of sufficient pathologic interest to be mentioned:

1. Murmurs arise more readily if the walls of the tube be thin than if they be thick.

2. If the inner surface of the tube be roughened, friction increases and murmurs arise more readily, requiring a less rapid current.

3. A much greater rapidity of current is necessary to give rise to murmurs in glass or brass than in yielding or distensible tubes (rubber tubes, intestines, veins).

4. Quicksilver causes murmurs more readily than water, water more readily than milk, milk more readily than blood mixed with water, heavy fluids more readily than light fluids, thin fluids more readily than tenacious fluids.

5. Sometimes the vibrations of the tube become so strong that they can be appreciated not only by the ear, but also by the sense of touch. They feel like sand running over the finger.

6. With a certain grade of rapidity of the current and narrowing of the tube a finer, more singing tone (musical murmur) can sometimes be heard.

7. Increased or diminished tension of the wall (by means of increased pressure of the fluid) has little influence upon the murmur so long as the rapidity remains the same.

8. If we gradually narrow a tube through which fluid is running, a murmur will appear after a certain degree of this compression. Increasing the compression will increase the intensity of the murmur up to a maximum, then diminish it, and finally cause it to disappear.

The diagrams make it plain that under the conditions which occasion current murmurs, eddies arise at the point in question. These can be plainly demonstrated by using a glass tube and suspending a light, insoluble powder (lycopodium) in the flowing liquid. It has been supposed that these eddies were the causes of the current murmur.[1] Such a supposition is, however, but partially correct, because the only parts which produce actual sound must be in permanent vibration, and fluids remain in permanent vibration only with difficulty; while in such irregular cavities as those of the heart and vessels such permanent vibrations would be hardly conceivable. In any case eddies in themselves have nothing in common with permanent vibrations. The fluid shares in the vibrations of the wall, but the common vibration of the two is due to the wall, not to the fluid. It is, however, clear that the eddies are an integral part of the entire process; and probably they are essential to the origin of permanent vibrations of the tube-wall. They must exist together. Thomas Weber has aptly compared the part of the fluid and the eddies to the rôle of the moving violin bow; the part of the vessel-wall vibrations to the rôle of the sounding string.

Valvular Murmurs.—Valvular Murmurs in General; Organic and Functional Valvular Murmurs.—To explain the elementary relations of valvular murmurs it is better, for the moment, to neglect the part played by the rapidity of the current.

Valvular murmurs may arise at any valve when the blood-current, either during systole or diastole, flows into an adjoining chamber through a narrow orifice. Such a result may happen in one of two different ways: either the valves do not open completely, forming a *stenosis*, or they do not close completely, and so allow a blood-stream flowing in an abnormal direction to escape through a narrowed opening, thus forming an *insufficiency* or *regurgitation*.

Anatomically, a *stenosis* is caused by adhesion of the individual segments of the semilunar or of the auriculoventricular valves, or else by a shrinkage of the orifice. *Insufficiency* of the valves arises from the shrinkage of the curtains in the long axis, from partial destruction or perforation of the valves, from tearing free of the entire curtain, or from uneven new deposits [vegetations.—Ed.], which mechanically prevent a perfect closure of the valves. In any of these cases we speak of an *organic* or *anatomic valvular lesion*.

Without being anatomically diseased, a valve may, however, be incapable of closing if the orifice at which it is inserted becomes dilated. This is called a *relative insufficiency*. The curtains no longer suffice to close the widened orifice, or the position of the papillary muscles is so distorted by the ventricular dilatation that the valves can no longer perfectly close. Widening of the orifice in relative insufficiency of the

[1] Heynsius is the chief advocate of this theory.

semilunar valves (*i. e.*, dilatation of the walls of the aorta or the pulmonary artery) depends upon increased blood-pressure, upon loss of elasticity of their walls (arteriosclerosis), or upon deposition of histologic elements in them (inflammatory swelling). On the contrary, relative insufficiency of the auriculoventricular valves, for the most part dependent upon a diastolic distention of the ventricle, signifies too great an influx of blood from the veins, or, with insufficient cardiac power, an incomplete emptying of the ventricle. If such relative insufficiencies be not permanent, but depend upon some transitory disturbance of function (transitory dilatation), they are called *functional relative insufficiencies.*

In contrast to the purely mechanical insufficiencies due to dilatation (relative insufficiency in the narrower sense) is the so-called "muscular insufficiency" (Friedreich) when there is no widening of the orifice. This is due to a lack of proper functioning of the papillary muscles, which prevents the normal closing of the valve. This failure may arise from muscular weakness (disturbances of compensation), in which case, however, it is usually combined with dilatation of the orifice, or from disturbances of innervation, *e. g.*, in chorea.

The blood-current producing the murmur in a valvular stenosis is directed normally; in an insufficiency, abnormally—flowing backward. So, without further explanation, it is apparent that a *murmur of stenosis* is heard during that phase of cardiac action in which the valves are opened; an *insufficiency murmur*, on the contrary, during that phase in which the valves should shut.

Compare here the following scheme:

	Systolic murmurs.	Diastolic murmurs.
Insufficiencies	of mitral,	of aorta.
	of tricuspid,	of pulmonary.
Stenoses	of aorta,	of mitral.
	of pulmonary,	of tricuspid.

Valvular lesions are, as a rule, accompanied by murmurs; yet not rarely decided lesions, which perhaps were only suspected during life from some other clinical conditions, are found postmortem in hearts that never gave a murmur. This is easily understood when we recall that a definite minimum of current rapidity for each grade of narrowing is essential to cause a murmur, and also that the narrowing must not be too pronounced (p. 328). Mitral stenosis, *e. g.*, may occur without a murmur, because the diastolic current is relatively too slow, since diastole lasts much longer than systole. For this reason a valvular lesion must be considered as a possibility in every case of heart disease, whether associated with a murmur or not.

Significance of the Timbre (Quality of the Sound) and of the Loudness (Intensity) of the Valvular Murmur.—We were formerly inclined to overvalue the diagnostic significance of the timbre of an endocardial murmur and to draw conclusions from it as to the conditions of the altered valves. It has, however, been proved that all conclusions based upon the rough, blowing, musical, whistling, or singing character of the murmur are entirely untrustworthy. Such a quality varies so much with the accidental configuration of the damaged valves that we deem it of very little importance. Nevertheless, the musical or scratching character of a heart murmur certainly argues against its being of accidental nature. (See p. 340 et seq.)

Even the *loudness of the murmur* does not necessarily correspond to the degree of a valvular lesion, as some physicians are still inclined to believe, for, as the experiments with the tubes prove (see p. 329, Law 8), a certain rapidity of current is requisite to bring out a maximum murmur through a definite narrowing. If the narrowing of the tube be too slight, the murmur is weak; if the narrowing be too pronounced, the murmur is, under some circumstances, still weaker, probably on account of the great loss of energy. In every valvular lesion, whether insufficiency or stenosis, as the defect increases the murmurs increase in intensity until a maximum is attained; then, despite further increase in the valvular defect, the murmur diminishes again. Now, it is not possible, in a given case, to determine from the character of the murmur whether the valve lesion (*i. e.*, the narrowed channel) has already passed or has not yet reached its acoustic maximum, so here, again, no sure inference can be drawn from the loudness of the murmur. Much more trustworthy conclusions are to be deduced from carefully heeding the various cardiac functions and from other methods of examination, particularly the estimation of the size of the heart.

How little the loudness of the murmur shows the severity of a valvular lesion is proved by the clinical fact that cardiac invalids with exceptionally loud murmurs may live for years, whereas others, with scarcely audible or even no murmurs, may very soon succumb to their malady.

Murmurs vary a great deal in the same patient, depending upon the kind of cardiac activity. Even a very brief medical experience teaches that the patient's condition is by no means always the best when the murmur is scarcely audible, but frequently the worst. The first essential for murmurs mentioned in our theoretic discussion, viz., current rapidity, easily explains this seeming inconsistence. If the patient's condition be good, a vigorous current is flowing through the diseased valve and the murmur is, therefore, strong and loud. If by weakening of the cardiac power the patient's condition be impaired, the current which causes the murmur is diminished, the murmur weakens, and finally even disappears. This sometimes makes the diagnosis of valvular lesions very difficult, especially because we generally examine patients when things are not going well with them. We must, therefore, often withhold our opinion until our treatment has improved the patient's condition sufficiently to bring out the murmurs; or we may temporarily increase the current rapidity and so bring out a suspected murmur by causing the patient[1] to execute some active movements augmenting the heart action.

A very loud murmur is only rarely accidental; so that although the loudness of a murmur is not necessarily a measure of its severity (p. 340 et seq.), still it is an argument against its accidental nature.

The influences external to the heart which modify the loudness of the valvular murmurs are the same as those affecting the heart tones. (See p. 316.)

We should always auscultate a patient in different positions, particularly standing and lying down. This is especially important in the determination of murmurs, because position has a great influence upon their character and intensity. Frequently a certain murmur can be heard only in the recumbent, another only in the erect, posture. This

[1] Up to a certain grade this is also possible in insufficiency.

cannot always be satisfactorily explained by the fact that the blood-current and the blood-pressure are decidedly influenced by posture. We will refer under the individual valvular lesions to the physical relations which apply to this point.

The Localization of Valvular Murmurs in Simple Valvular Lesions.—The essential requisite for an exact diagnosis of a valvular lesion consists in localizing the murmur, *i. e.*, in recognizing at what valve it arises. This is not always easy, because murmurs are heard not only where they arise, but by transmission elsewhere. In general the same rules apply to the localization of murmurs as to the localization of tones (p. 309 et seq.), *i. e.*, murmurs of the mitral should be heard at the apex; of the tricuspid, at the lower end of the sternum; of the pulmonary, in the second intercostal space, to the left of the sternum; and of the aortic valve, in the second intercostal space, to the right of the sternum.

Exceptions to these rules are so numerous that some explanation seems necessary. If the heart chambers at either side of a narrowing be of unequal size, a stronger (louder) murmur arises over the larger than over the smaller chamber. (See Weber's experiments, p. 328.) If the murmur originate at some distance from the chest-wall, it may be heard more plainly at a spot upon the thorax quite remote from the point of projection of its place of origin. This depends upon its so-called *transmission* through the medium of the blood-stream, either with or against the current. If transmitted in the direction of the stream, the murmur is louder than if transmitted against the current, just as "the wind carries the sound."

1. *Systolic murmurs arising at the aortic valve* are ordinarily heard loudest at the aortic area (the second right intercostal space), because here the aorta lies near the thorax-wall, and because the blood-current causing the murmur is directed to that side. They are transmitted, however, strongly upward to the carotids; this latter fact may be utilized in doubtful cases in order to distinguish between mitral insufficiency and aortic stenosis. Not infrequently systolic aortic murmurs are heard plainly over the left ventricle as well, *i. e.*, at the apex. This is simple enough to understand, because they arise also in the left ventricle (p. 327).

2. Ordinarily, the *diastolic murmur* of *aortic insufficiency* is not heard so plainly at the aortic area as it is further below, nearer the apex. Perhaps most frequently it is loudest at the middle of or to the left of the lower part of the sternum. The reasons are: first, that the aortic valves are situated deeply, at a distance from the aortic area (see p. 309); second, that the murmur arises principally during diastole in the dilated left ventricle (p. 329); and third, that the current causing the murmur is directed from the aorta to this chamber. The murmur of aortic insufficiency is also frequently to be heard over the neck vessels.

3. The *systolic murmur* of *mitral insufficiency*, like the mitral tone, is ordinarily heard best at the apex, and not over the location of the mitral valve. Despite the location of the valve and the better transmission of the murmur through the blood-current, which is directed upward, the upper part of the left ventricle is so completely covered by the right ventricle and lung that the murmur is heard most plainly at the apex. Another reason is that, at the beginning of systole, the left ventricle is much larger than the auricle, and so a louder sound is heard over the

ventricle (*i. e.*, apex) than over the auricle. There are instances, however, where the systolic mitral murmur is best heard at the base of the heart, in the vicinity of the left auricle, at the projection spot of the mitral valve, in the third intercostal space, to the left of the sternum. Probably this occurs chiefly when there is a marked dilatation of the left auricle. The lung is then pushed aside and the left auricle exposed, which naturally facilitates the appreciation of the murmur over it and the mitral valve. Besides, the current causing the murmur is directed to the region of the left auricle. Marked dilatation of the left ventricle also pushes the maximum point of the systolic murmur from the heart apex upward, because such a dilated left ventricle crowds the right ventricle and the lung and applies itself more completely to the thorax, so that the region of the mitral valve and the left auricle is exposed.

4. In *mitral stenosis* the direction of the current causing the murmur is an especial reason for the sharp localization of the diastolic murmur of this valve lesion (even more than the mitral tone, see p. 309) at the apex. If faint, the diastolic murmur of mitral stenosis can sometimes be heard only just outside the apex. This is especially applicable to the so-called presystolic murmur (see p. 335), in which case there is also another reason, viz.: the left auricle during presystole is small and the left ventricle large. But a pure diastolic mitral murmur (p. 335) is frequently heard best over the auricle, because it arises at the beginning of diastole, when the left auricle is wide, and the left ventricle, in comparison, is then narrower.

5. The *systolic murmur of tricuspid insufficiency*, in spite of the direction of the current upward, is heard most distinctly at the tricuspid area, the lower end of the sternum or somewhat to the right of it, because here the right ventricle as well as the right auricle lies near the thoracic wall (Fig. 120). Other systolic murmurs, excepting perhaps the systolic murmur of the rare pulmonary stenosis, are not plainly transmitted to this spot.

6. The *diastolic murmur of tricuspid stenosis*, a rare lesion, has its maximum intensity at the tricuspid area, the lower end of the sternum, because the current from the affected valve above is directed toward this spot, and because both cavities, right auricle and right ventricle, here lie close to the thoracic wall.

7. The *systolic murmur of pulmonary stenosis* is auscultated at the pulmonic area (the second left intercostal space) and over the right ventricle.

The murmur of pulmonary stenosis is frequently heard over the greater part of the anterior surface of the heart, because the right ventricle is ordinarily so dilated in this lesion that it occupies most of this area; and because (p. 329) the murmur arises not only at the stenotic valve, but also over the right ventricle. This is a point which should be carefully heeded to prevent confusion in diagnosis.

The pulmonary stenotic murmur should be plainly transmitted into the interior of the lung; it should also be heard very distinctly beneath the left clavicle (where aortic murmurs are only faintly transmitted), or behind, between the shoulder-blades, and, in contrast to the murmur of aortic stenosis, it is either not transmitted at all, or only very slightly, into the neck vessels.

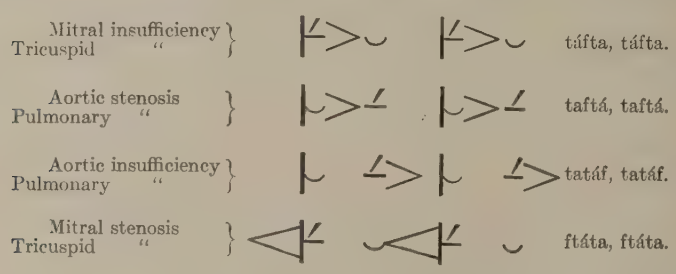
8. The *diastolic murmur of pulmonary insufficiency* is auscultated at the pulmonic area. Like the murmur of aortic insufficiency, it can,

however, be heard more plainly over the lower end of the sternum, because it arises essentially in the right ventricle (p. 329), and because the blood-stream producing the murmur is directed downward. Unlike the aortic murmur, it is not transmitted into the neck vessels.

Some of the above rules do not apply if the heart be pushed from its normal position to any extent. This must happen frequently, because valvular lesions cause marked dilatations and alterations of individual heart chambers.

Exact Time Relations of the Valvular Murmurs to the Heart Tones; Simple Diastolic Murmurs, and Modified Diastolic or Presystolic Murmurs; Prediastolic Murmurs; Distinction Between the Systolic Murmurs Arising Over the Arterial Orifices and Those Over the Auriculoventricular Orifices.—The heart tones are frequently heard, as well as murmurs, both over the intact valves and over the diseased valves which give rise to the murmur. In the first place, the tones may be transmitted from one of the unaffected valves; in the second place, the walls of the heart and of the great vessels participate in forming the tones; and in the third place, the diseased valve is hardly ever destroyed, and so its tone may still be produced (p. 318 et seq.). By listening to the tone, a skilled examiner can determine the phase of cardiac action to which a certain murmur belongs. Everything which occurs between the beginning of the systolic tone and the next succeeding diastolic tone belongs to systole; and everything which occurs between the diastolic tone and the next systolic tone belongs to diastole. So a murmur, though very close to the systolic tone, and quite remote from the diastolic tone, is still diastolic so long as it occurs before the beginning of the systolic tone, *e. g.*, a presystolic murmur is really diastolic.

The murmurs of the different valvular lesions, together with their tones in their proper time relations, are represented in the following scheme:



The vertical lines mark the beginning of systole. This scheme shows us that the acoustic picture of a valvular lesion is a very varying one. The beginner can represent the tones sufficiently accurately by the syllables "ta-ta," the murmurs by the letter "f," as in the scheme.

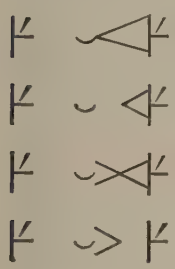
Although it is plain that members of each pair of these eight valvular lesions are acoustically related, yet there is less confusion than one might suppose, because the murmur of every lesion has a definite point of maximum intensity, and every lesion occasions distinctive

circulatory disturbances, as well as many other symptoms. A differentiation is thus possible in almost all cases.

Most murmurs are represented by the diminuendo sign, because their intensity is greatest at the beginning of the phase of cardiac action to which they belong. The reason is that the blood-current is then most rapid. The diastolic murmurs of the auriculoventricular stenoses are the only exceptions, because the auricular contraction increases the current rapidity and they are represented by the crescendo sign.

It should be noted that an actually uniform crescendo may occur during the progressive contraction of the auricle and the concomitant dilatation of the ventricle. The murmur really increases during the course of the auricular systole on account of the increasing difference between the sectional area of the contracted auriculoventricular orifice and that of the ventricle. (See Weber's Laws of Origin of Murmurs, p. 328.)

Tricuspid stenosis is so rare as to be practically neglected, so that a *presystolic accentuation at the end of the murmur* is practically pathognomonic of mitral stenosis. In puzzling cases this very characteristic accentuation at the end of the murmur sometimes aids in distinguishing the phases of cardiac action. Although theoretically it is not a uniformly regulated crescendo, the duration of the whole sound is so short that the ear receives the impression that it is.



Presystolic accentuation of the diastolic murmur.

Pure presystolic murmur (most common).

Diastolic murmur accentuated at the beginning and at the end of diastole.

Pure diastolic murmur (least common).

The *pure presystolic murmur* is still more common in mitral stenosis. This is represented by a short crescendo sign, for there seems to be an actual pause between the diastolic tone and the murmur. Another modification consists of an *accentuation both at the beginning and at the end of the murmur*. This depends on the fact that the blood flows into the empty ventricle with greater rapidity at the beginning of diastole than during its middle period, when the difference of pressure between the auricle and ventricle has been to a great extent equalized. The last modification, the *pure diastolic murmur*, is the least common. The murmur follows the diastolic tone directly and then decreases in intensity without any subsequent presystolic accentuation. These four varieties of murmurs due to auriculoventricular stenosis can be illustrated by the preceding scheme.

All these modifications of the murmurs obviously depend upon the varying relations of the factors which influence the intensity of the murmur at each moment, *i. e.*, upon the degree of the stenosis and upon the rapidity of the blood-current. Therefore it is easily understood that

in one and the same case, depending upon the rapidity of the cardiac action, we hear one modification at one time and another modification at another time.[1]

We have yet to mention a characteristic sort of valvular murmur, designated as a *prediastolic murmur*, to be heard, of course, toward the end of systole. It may be expressed symbolically thus:

and reproduced by the sound "tá-fta." It arises at the auriculoventricular valves, and is limited to the end of systole, probably because at the beginning, and perhaps even during the greater portion, of systolic contraction the valves remain closed, and only relax and bend toward the auricle when the intraventricular pressure has reached a certain height, *i. e.*, shortly before or during the time of expulsion. This may be due to an incomplete contact of the curtains, or to an anomaly in the chordæ tendinæ or papillary muscles. If this supposition be correct, a prediastolic murmur would argue for a moderate grade of auriculoventricular insufficiency, which would be differentiated from the ordinary insufficiency by the fact that the closure time is in part or entirely retained. Ordinary systolic murmurs may be either accidental or organic, whereas prediastolic murmurs always depend upon actual auriculoventricular insufficiency, whether relative or anatomic. It is, however, also conceivable that an insufficiency of the auriculoventricular valve produces a prediastolic murmur because the origin of the murmur is especially favored by the decided dilatation of the auricle at the end of ventricular systole. (According to Thomas Weber's *Fundamental Laws*, p. 328.)

We must call attention, finally, to the difference first noted by von Noorden between systolic murmurs arising at the greater vessels and those arising at the auriculoventricular orifices. With a moderate degree of auriculoventricular insufficiency the systolic murmur begins exactly at the commencement of systole, with the first tone, because the insufficiency deprives the ventricle of a proper closure time, and because the blood, overcoming the low auricular pressure, regurgitates, even at the very beginning of the ventricular contraction. It is otherwise with aortic and pulmonary systolic murmurs. Here the murmur appears first at the beginning of the expulsion time, *i. e.*, after the closure time is completed, the intraventricular pressure overcomes the aortic pressure. This causes a delay of the systolic murmur as contrasted with the first tone; and though slight, a skilled ear can frequently appreciate and make use of it in diagnosing systolic murmurs of

[1] It cannot be decided absolutely in a given case that these modifications are sure diagnostic signs. The question should be tested at autopsy, in order to determine whether (supposing, of course, a normal current rapidity, *i. e.*, a compensated case) the pure diastolic murmurs correspond to the slightest, the diastolic murmurs with the presystolic accentuation to the moderate, and the pure presystolic murmurs to the most severe, grades of stenosis. Certainly this explanation is partially correct, since it is plain that with a moderate stenosis the current giving rise to the murmur will be maximal at the beginning of diastole and at its end (during the auricular contraction); whereas, with a very marked stenosis, it requires an exceptionally active contraction of the auricle to force a sufficiently rapid current into the ventricle in order to give rise to a murmur.

Sometimes in one and the same case a pure diastolic murmur is heard at the base of the heart, whereas at the apex most of what is heard is the presystolic portion (p. 333, Law 4).

the great vessels from those of the auriculoventricular orifices.[1] The distinction may be designated symbolically thus:

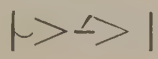
Mitral and tricuspid insufficiency. Aortic and pulmonary stenosis.

Only very close attention will detect this distinction. The closure time between the systolic tone and the murmur is so short (0.07 to 0.14 second, according to Martius[2]) that the interval cannot be detected as a distinct pause, but merely gives an impression of a somewhat less close connection between the murmur and the tone.

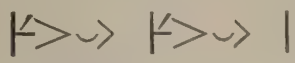
We need not fear confusion with a prediastolic murmur, because the latter is separated from the systolic tone by a longer pause, which is very plain; and because the succeeding diastolic tone follows so closely that it seems a part of the murmur.

Combinations of Murmurs from Multiple Valvular Lesions.—The same valve is frequently both narrowed and insufficient; hence we may meet with the following combinations of murmurs and tones:

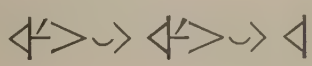
Mitral insufficiency and stenosis
Tricuspid insufficiency and stenosis { ftáfta ftáfta

Aortic insufficiency and stenosis
Pulmonary insufficiency and stenosis { taftáf taftáf 

When several valves are affected at the same time, the murmurs, if loud enough, may be transmitted over the entire heart, *e. g.*, with a combination of mitral and aortic insufficiency. In case the aortic murmur is transmitted to the apex, we may hear the following:

 táftaf táftaf

If there be a mitral stenosis in addition, we shall hear at the apex this modification:

 ftáftaf ftáftaf

Method of Localizing Murmurs in Multiple Valvular Lesions; Maximum and Minimum Points.—If several valves be diseased, and if one of them be doubly so, *i. e.*, with a stenosis and insufficiency, the murmurs will be transmitted in all directions, and the diagnostic picture will become so complicated that it may be very difficult to determine where each murmur really arises and where each one is to be heard merely by transmission. If, for example, a systolic murmur be heard at two orifices, *e. g.*, at the mitral and the aortic, it is very difficult to say whether the murmur at the aorta depends upon an aortic

[1] To detect this delay one must listen somewhat below the auscultation point for the arteries, in order to be sure of comparing the time of the systolic murmur with that of the first tone. Over the great vessels one may be easily confused by the "expulsion tone" (p. 322), which, of course, follows the murmurs of the great vessels *without* delay.

[2] Zeit. f. klin. Med., 1888, vol. xiii.

stenosis or is merely the transmitted mitral murmur. It is very easy to make a mistake in either direction.

The best way to solve such a problem is first to represent upon a chest chart, as in Fig. 159, the two murmurs, the tones, and the cardiac dulness, and then to decide, after very careful auscultation, whether any difference in the acoustic quality of the two murmurs can be detected.

Should the two murmurs exhibit a slight difference in quality, for example, one rough, the other smooth; one musical or whistling, the other blowing, it is probable that each murmur has a separate origin. But one must be somewhat cautious in drawing this conclusion, as the quality as well as the intensity of a murmur may, of course, be slightly altered by transmission.

If no distinction in quality can be made out, a careful auscultation will usually determine that the murmur is heard more clearly or

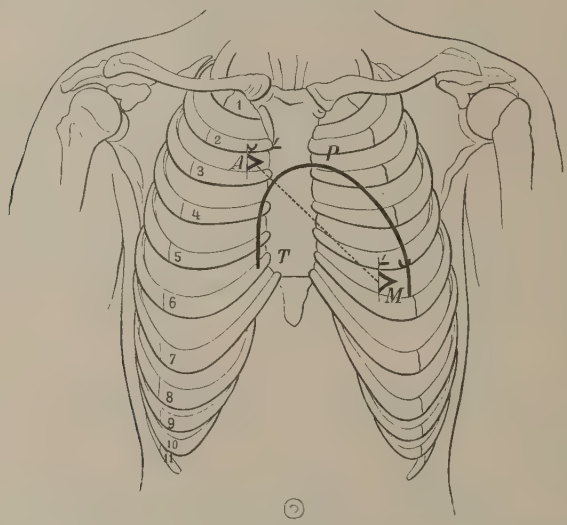


Fig. 159.—Diagram to illustrate the method of localizing murmurs.

intensely at one point than at another. Then the following possibilities will exist:

1. If the murmur be equally intense at both orifices, it is probable that a separate murmur arises at each spot, because transmission generally deprives a murmur of some of its intensity. Very loud murmurs might, however, be heard over the entire heart with equal intensity.

2. If the murmur be less intense at one orifice, *e. g.*, much less distinct over the aortic than over the mitral, the weaker murmur will generally be due to transmission. This is not necessarily so, however, as a faint murmur might arise from the aortic, and a very loud murmur from the mitral. To clear up the difficulty, we should auscultate from the one orifice to the other along the line *A M*, Fig. 160, I. If the murmur *A* be merely transmitted from *M*, its intensity will steadily increase from *A* to *M* (represented diagrammatically by a wedge-shaped

figure, whose breadth at each spot is a measure of the intensity of the murmur). But if, on the contrary, in auscultating from *A* to *M*, we find that the intensity of the murmur at first diminishes, reaches a minimum somewhere between *A* and *M*, then increases again up to a second maximum at *M* (Fig. 160, II), so that there are two maximal points, then, even though the murmur be weaker at *A* than at *M*, we can be sure that there are two different murmurs.

Supposing, as is so often the case, that the systolic murmur can be heard not only at *A* and *M*, but also (Fig. 160, III and IV) at *T* and *P* (tricuspid and pulmonary areas), the question arises whether at these four points we have to do with transmitted or original murmurs. Here we must again carefully heed the resonating quality and then auscultate along the lines *A P* and *A T*, *M T* and *M P*. The relations of in-

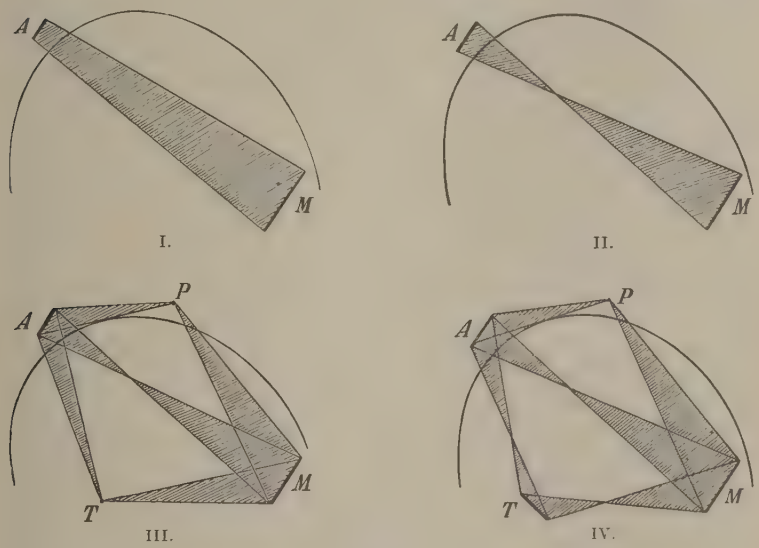


Fig. 160.—Diagram of the relations of transmission of cardiac murmurs: Maximum and minimum points.

tensity expressed in Fig. 160, III, show that the murmurs *P* and *T* are merely transmitted from *A* and *M*, whereas those in Fig. 160, IV, show that separate murmurs arise at *A*, *M*, and *T*, but that the murmur at *P* is only transmitted.

In this way the beginner learns to orient himself concerning the points of origin of murmurs in complicated valvular lesions. The important point is merely to proceed systematically. If both systolic and diastolic murmurs be present, first analyze the diastolic, not heeding the systolic, and later proceed in the same way with the systolic. With diastolic murmurs the problem is often simplified by remembering that modified diastolic murmurs, *i. e.*, presystolic or presystolic accented murmurs, can arise only at the auriculoventricular valves. Another almost constant law is that aortic murmurs, especially the systolic variety, are strongly transmitted to the neck vessels.

We hardly need mention that no importance should be attached to slight differences of intensity, because they may arise from causes we do not yet comprehend. The diagnosis of a combination of an aortic and a mitral murmur which occupy the same phase of heart action requires especial attention. We not infrequently find two plainly marked maximal points with an intermediate minimum, as in Fig. 160, II, due to a single murmur; because murmurs arising from the left heart are best transmitted to the surface wherever the left heart is most closely approximated to the thoracic wall, viz., in the region of the aorta and at the apex, whereas at other places the superimposed right ventricle makes the appreciation more difficult. If a murmur be musical and of the same quality and pitch both at *A* and *M*, this assumption is pretty safe. The resonating quality in any case should, therefore, be closely studied. The above-mentioned difficulties render it practically impossible for auscultation alone to differentiate between the single and double origin of a murmur; hence, all the other relations should be carefully heeded.

Other Methods of Examination.—From what has been said above, it might appear that the various valve lesions could be perfectly differentiated by auscultation alone, but this is not so. As we shall see in the next section, murmurs of the same character as those due to valvular lesions may occur without the existence of any lesion, and alterations in the circulation, as well as the resulting variations in the size of the heart, are quite as significant as the murmurs. Besides, to localize the murmurs properly, as outlined above, we must have an exact knowledge of the heart's size and position. The median line of the body is selected as a starting-point, but the size and position of the heart in reference to the median line are, of course, altered by the lesion, and hence for the localization of the murmurs we require other methods of examination, especially percussion. (See later under the Individual Lesions.)

So-called Accidental Heart Murmurs.—Many cardiac murmurs depend upon relative or functional insufficiencies of the valves, and are called *relative* or *functional* murmurs. They generally depend upon a dilatation of the valvular ring or a lack of proper functionating on the part of the papillary muscles (p. 330 et seq.). To all intents and purposes we can consider them under the same heading as organic murmurs, and whatever we have said thus far under the latter head will apply to these functional murmurs.

Accidental murmurs, on the contrary, are entirely independent of the valvular mechanism, and, although acoustically they cannot be distinguished from the murmurs of true valvular lesions, at autopsy the valve is found to be perfectly normal.

They are frequently called *inorganic* or *functional* murmurs. "Functional" seems to the author as incorrect a term as "inorganic," because real valvular murmurs may depend upon purely functional disturbance, and some accidental murmurs have an anatomic origin. For example, anemia is certainly an anatomic disease. Accidental murmurs have also been described as "anemic." This is inaccurate, because all accidental murmurs do not depend upon anemia, nor are all anemic murmurs accidental (relative insufficiency occasioned by anemia, p. 342). The only way to escape this confusion is to distinguish *organic valvular murmurs sharply from accidental murmurs*, and to separate *relative insufficiency murmurs from accidental murmurs* and to classify these relative insufficiency murmurs with the true organic murmurs.

Although the real origin of accidental murmurs still remains unproved, the author will attempt to state his own views upon the subject in what follows.

Accidental murmurs are, with few exceptions, systolic in time. They are not at all uncommon in health, and are then heard, for the most part, either at the apex or over the pulmonary artery. Autopsies furnish negative results, so that their origin is conjectural. Acoustically, they are not essentially different from valvular murmurs; therefore we assume that they, too, are current murmurs arising in con-

formity with the laws applied to valvular defects. In the normal heart the experimental conditions (p. 327 et seq.) essential to valvular murmurs are surely present, and it is certainly more astonishing that ordinarily the blood flows through the heart without murmur than that murmurs may arise from perfectly normal hearts. Consider the irregularly formed inner surface of the ventricles, the resulting chances for friction, and the alteration in cross-section in the connecting portion between the ventricles and aorta or pulmonary artery. Indeed, it is almost more logical to attempt to explain how it is possible for tones, and not murmurs, to arise over the normal heart. Perhaps it is because the normal blood-current is not rapid enough to give rise to murmurs. Accidental murmurs would then depend upon an increased rapidity of the blood-current. The latter, in so far as it concerns systole, depends apparently upon the rapidity with which the ventricle contracts and upon the mass of blood to be emptied, *i. e.*, upon the amount of diastolic filling of the heart. Stolnikow[1] has demonstrated experimentally that the velocity of the blood-current may vary a great deal. In one experiment he found that the maximum was sixteen and one-half times greater than the minimum current velocity.

How completely the ventricle is filled during diastole appears to be of especial importance. For v. Frey and Krehl[2] found, in their experiments, that slowing the heart action, and thereby increasing the diastolic filling of the heart (vagus irritation or suffocation), only slightly prolongs the duration of the ventricular contraction. As a direct consequence, the pulse is slowed and the velocity of the current is increased. But, so far as the author knows, no direct experiments show that the current-velocity with low arterial pressure, *i. e.*, with slight resistance to systole, or with altered innervation of the heart, can be considerably accelerated without altering the frequency of the beat or the diastolic filling. Nevertheless, this does seem probable.

Accidental murmurs may therefore arise if the diastolic filling increase while the expulsion time remains constant, or if the ventricle contract more rapidly while the diastolic filling remains constant. The latter possibility seems possible, because accidental systolic murmurs, like many valvular murmurs, sometimes arise when the heart action has been excited or made rapid. But even so, this does not explain why they are ordinarily to be heard at the pulmonic area or over the left ventricle, and very rarely at the aortic area or over the right ventricle, unless it is on account of the varying anatomic configuration of the right and left ventricles and of the conus arteriosus.

They do not readily appear during diastole, because the velocity of the current during diastole is, on account of the longer duration of the latter and its weaker power, much less than the systolic. Besides, during diastole the current does not encounter any such alteration in the cross-section of the heart as it does during systole in its entrance into the aorta or pulmonary artery.[3] Experience with mitral stenosis shows that the conditions in the interior of the heart are not especially favorable for the formation of diastolic murmurs, for frequently the diastolic murmur can be heard only during the presystolic accentuation of the auriculoventricular current (p. 335). Again, no other valvular lesion is so apt to run its course without a murmur as mitral stenosis (pp. 328 and 330).

Accidental murmurs appear most often when the ventricle contracts quickly; therefore we should expect them most frequently in strong people with good blood-pressure, and yet the reverse of this is true. To this objection the author can only reply that rapid contractions of the ventricle are in no way to be identified with high blood-pressure. Since the blood-pressure furnishes a resistance to the cardiac contraction, it is, on the contrary, probable that the ventricle would contract more rapidly with low pressure than with high. No special researches, so far as the author knows, have been made upon this point. To claim that because high blood-pressure increases the friction it favors murmur formation is the same as saying that the pressure, in so far as it does not influence the rapidity of current, has little or no effect upon murmur formation. (See the experiments of Weber, Heynsius, Nolet, and Thamm, pp. 327–329.)

The above explanation of accidental murmurs applies particularly to healthy individuals, in whom they very frequently occur. Lüthje has shown that, in the majority of children from ten to fourteen years of age, an obviously accidental systolic murmur can be heard at the pulmonic area. This may be due either to a quickened systole at that age, or to the difference in lumen between the ventricle and the pulmonary artery, which is especially marked in comparison with the size of the child, a condition to which Lüthje has given the name of "relative pulmonary

[1] Arch. f. Anat. u. Physiol., Physiologic Part, 1886. [2] Ibid., 1890, No. 47.

[3] The difference of cross-section between the veins leading to the heart and the auricle is much less than that between the distended ventricle and its efferent arteries.

stenosis." In either case the essential factor is the increased rapidity of flow in the pulmonary artery. But this explanation also applies particularly to those pathologic conditions in which accidental murmurs so frequently occur, *i. e.*, weakness, fever, and anemia. In so far as general weakness is combined with low arterial pressure, its effect has been already discussed. In fever the acceleration of the pulse and the decreased tension of the arteries, expressed by the sphygmogram and in the usually lowered blood-pressure, would make the supposition of a rapid expulsion of the blood from the heart probable. Rüedi's demonstration of the so-called "tachogram" of the fever pulse also adds some weight. In regard to anemia, we must distinguish between the acute anemia of hemorrhage and the chronic anemias or oligochromemias; in the former the low blood-pressure, in the latter the diminished cohesion or viscosity of the blood, probably occasions an increased flow from the heart by lessening the resistance. Cohnheim proved that artificial hydremia accelerates the blood-current, thus explaining the "venous hum" of chlorotics. (See p. 350 et seq.) In chlorosis and other oligochromemias the diminished cohesion or viscosity of the blood may also favor murmur formation (according to Law 4, p. 329).

The hypothesis advanced by many authors, that accidental murmurs depend upon an abnormal facility of vibration of the valves and of the arterial walls, seems to the author absolutely inexplicable. Whoever appreciates the fundamental difference between the much prolonged acoustic character of a murmur and the stroke-like character of a heart tone will hardly be satisfied with the supposition that the tension of even a relaxed and irregularly vibrating membrane can produce such a blowing murmur.

Special roughness of the walls through which the blood-current passes (Law 2, p. 328), independent of valvular disturbances, does probably play a certain part in the origin of accidental murmurs, as in atheroma of the aorta and of the endocardium. This explanation evidently cannot apply to accidental murmurs in general, however, because accidental murmurs are only rarely heard loudest over the aortic orifice; because the pulmonary artery is almost never atheromatous, and because cases presenting accidental murmurs during life show no atheroma postmortem. In certain exceptional cases supposed accidental murmurs are nothing more than systolic vesicular breathing (p. 284).

So much for accidental systolic murmurs. The conditions in the heart itself are very unfavorable for producing accidental diastolic murmurs; but in rare cases a simple diastolic murmur with its maximum over the aorta, and so easily confused with an aortic insufficiency murmur, does appear without being dependent upon any valvular lesion. In anemic individuals[1] such a murmur is to be regarded as the diastolic accented portion of the venous hum, transmitted from the jugular veins to the adjoining portions of the innominate veins and the vena cava superior to the heart (p. 350). By auscultating from the aorta upward to the jugular vein, one can generally convince one's self that the diastolic murmur, heard perhaps loudest over the aorta, gradually merges above into the rhythmic diastolic accentuation of a continuous venous hum. According to the author's experience, the occurrence of both these types of accidental murmurs is limited to the severest cases of oligochromemia (15 to 25 per cent. hemoglobin); and this naturally facilitates the diagnosis.[2] In general, however, diastolic accidental murmurs are rare; when diastolic, a murmur is nearly always valvular.

The author recently saw a case where a weak diastolic murmur at the aorta, plainly heard, though only during inspiration, led him to a diagnosis of slight aortic insufficiency, although the typical signs of a pulsus celer (arterial tones, capillary pulse, Duroziez's murmur, etc.) were absent. The autopsy, however, showed no

[1] Sahli, Correspondenzbl. f. Schweizer Aerzte, 1885.

[2] The author has, however, seen an instance of a very strong accidental diastolic murmur referable to a venous hum when the hemoglobin was reduced only to 55 per cent.

aortic insufficiency, but the presence of sharp, rough, chalky excrescences on the cusps of the valve, which evidently caused the murmur through eddies at the moment of diastolic stretching. So the accidental diastolic murmurs may be due to anatomic causes which do not affect the valvular function.

Another variety of accidental diastolic murmurs is the presystolic. They are rather rare, and have not before been described. They are probably caused by the presystolic acceleration of the blood-current. Like the murmur of mitral stenosis, with which they may be easily confused, they may be appreciated by palpation. They are due less to an anemic condition of the blood than to an increased contraction of the auricle, as is shown by the fact that they often occur without systolic murmurs or the venous hum.

The most practical points for distinguishing accidental from valvular murmurs may now be profitably reviewed. A murmur may be rightly considered accidental if nothing further point to a valvular lesion, *i. e.*, no preceding etiologic factor, such as inflammatory rheumatism, no abnormality of the pulse or of the circulation, no abnormality of the tone intensity, and no demonstrable dilatation of any cardiac chamber. Anemia, fever, atheroma, or a venous hum favors the diagnosis of an accidental murmur. Still, not every murmur heard over an anemic individual's heart is necessarily accidental; for relative insufficiencies are very often caused by anemic dilatation of the heart, and can be distinguished from anatomic valvular lesions only by the fact that they diminish or disappear with the improvement of the anemia. They are limited to the mitral and tricuspid, and are governed by the same diagnostic rules as the anatomic varieties. (See the Special Diagnosis of Mitral and Tricuspid Insufficiencies.) Location of the maximum point of a doubtful systolic murmur over the pulmonic valve argues in favor of its being accidental. Lüthje called attention to the fact that such murmurs are usually stronger during expiration and may even disappear during inspiration. He makes use of this fact to support his theory that they are due to "relative pulmonary stenosis" (see p. 341), since during expiration the lumen of the pulmonary artery is decreased. The accidental murmurs of atheroma, in accordance with the anatomic seat of the atheroma, are usually localized at the aortic orifice, but also frequently at the apex. Though signifying no valvular lesion, they are really of serious import, because they depend upon anatomic changes which may later occasion fatal disturbances, with or without producing a valvular defect.

Simple accidental diastolic murmurs are exceedingly rare, are almost always associated with a venous hum, very often with a systolic murmur, and are generally confined to the most severe types of anemia (oligochromemia) (see, however, p. 342).

The purely accidental presystolic murmurs may be distinguished from the murmurs in auriculoventricular stenosis by: (1) the changes in size of the heart accompanying the latter, and (2) the hard quality of the tone following the murmur, due to the rigidity of the valves in these lesions. (See p. 318.) But confusion may result if the heart action be excited beyond the normal, and a strong contraction of the auricle, causing a presystolic murmur, precede or be combined with an increased contraction of the ventricle accentuating the systolic tone.

It is questionable whether accidental murmurs can really be distinguished by any acoustic peculiarity from valvular murmurs. In general

they are not so loud as the valvular (see p. 331); nevertheless, we do hear very loud accidental murmurs, and, conversely, faint valvular murmurs, even in serious lesions. Similarly, the particular quality of a murmur, its blowing, scraping, or musical nature, is not distinctive, although the two latter characteristics generally depend upon some abnormal configurations of the cardiac cavities or orifices and rarely appear with purely accidental murmurs. The prediastolic character of a systolic murmur argues with some certainty against its being accidental, and in favor of a mild insufficiency of the auriculoventricular valve, which gives rise to the murmur only at the end of systole. (See p. 336.) A prediastolic murmur, according to this, would never be accidental. (See p. 336.)

Influence of Breathing Upon Endocardial Murmurs.—Whether valvular or accidental, endocardial murmurs are influenced by the phases of respiration in numerous ways. On the one hand, the extent to which the lung overlaps the heart is variable, depending upon the different phases of breathing; on the other hand, the breathing favors or hinders the current of blood through the heart.

So far as the overlapping of the lung is concerned, inspiration always weakens a murmur, because the heart is then more perfectly covered by the lung; expiration, on the contrary, intensifies it. The effect of breathing upon the blood-current is more complicated. (See p. 134 et seq.) The entrance of blood to, and the exit from, the right heart is always favored by inspiration. In the left heart it depends upon the rapidity of breathing. During rapid breathing the entrance to, and the exit from, the left heart, in consequence of the increased capacity of the pulmonary vessels and of the retention of more blood in the lungs, is hindered by inspiration. With slow, deep respiration, however, this influence can be noted only during the first half of inspiration, because in the second half the dilatation of the pulmonary vessels diminishes the resistance in the pulmonary channels, and so must favor the passage of blood through to the left heart. Expiration works in exactly the opposite way. It retards the blood-current through the right heart somewhat, because it diminishes the negativity of the intrathoracic pressure. Yet this influence is insignificant so long as expiration is merely passive. For the left heart the effect of expiration depends upon whether it be quick or slow. With slow breathing the first part of expiration aids the flow by compressing the pulmonary vessels, while the second part hinders the filling of the left heart by increasing the resistance in the pulmonary circulation. With quick breathing, on the contrary, only the first effect of expiration is felt, and the filling of the left heart is improved. This influence is sometimes very plainly observed in valvular lesions, since any increased current through a cardiac orifice necessarily intensifies a murmur arising there. Very important points for differentiating right- and left-sided valvular lesions will sometimes be furnished by carefully heeding these facts about the influence of quick breathing. It may be further mentioned that the Valsalva experiment (see p. 346) directly diminishes the endocardial murmurs of the right heart by inhibiting the venous current. It also diminishes the murmurs of the left only after an initial but transitory increase. This brief intensification is due to the pressure suddenly exerted upon the pulmonary vessels.

Paracardial Murmurs

Under this title are included all murmurs synchronous with the heart action which depend upon changes outside of the heart chamber, *i. e.*, in the pericardium or its immediate neighborhood. They include—(1) the pericardial rub; (2) the pleuropericardial rub; (3) the precordial emphysematous murmur; (4) the pericardial splashing.

Pericardial Rub.—Analogous to the pleural, the pericardial rub arises from the rubbing of the two pericardial surfaces when roughened by the deposition of inflammatory fibrinous or connective tissue, by tubercles, by tumors, or by abnormal dryness (in cholera). Pericardial rubs present exactly the same acoustic varieties as pleural rubs, *e. g.*,

they are sometimes finely creaking, sometimes crackling, sometimes scratching. Fine pericardial rubs, caused by an exceptionally slight roughness of the pericardium, are sometimes confused with endocardial murmurs. To make a diagnosis in such cases (as well as conversely in exceptionally rough endocardial murmurs), it is very essential to pay close attention to the phases of cardiac action. Endocardial murmurs conform most accurately to phases of cardiac action, coinciding with either the systolic or diastolic tone; pericardial murmurs, on the contrary, occur half-way between the tones, overstep the boundary between systole and diastole, or even quickly change phases, which endocardial murmurs never do. Sometimes pericardial murmurs are to be heard as a continuous scratching, which is merely intensified during the phases of cardiac activity. All this is perfectly comprehensible when we consider that the point of time during which a pericardial murmur is to be heard depends much less upon the phase of the heart action than upon the chance position of a roughness, which may alter its form and extent within a few hours. In explaining why the systolic part of the pericardial murmur does not exactly tally with the beginning of systole, Geigel noted that the greatest systolic excursion of the surface of the heart, as compared to its pericardium, does not occur during the closure, but during the expulsion time of systole, and, the author believes, even at the termination of the latter period.

We make use of the sign ⩘⩘ to describe and picture symbolically the pericardial murmurs. The height of the teeth expresses the intensity of the murmur at a given moment. The following diagrams exhibit different types of pericardial murmurs (see also p. 327):

Pericardial rub in the middle of systole and in the middle of diastole.

Pericardial rub systolic in time but also prolonged into diastole.

Continuous scraping pericardial rub, intensified in the middle of systole and in the middle of diastole.

Though pericardial murmurs may arise from the entire pericardium, the rubbing of the anterior surface of the heart is all that is usually heard, and more particularly of that portion uncovered by the lung or overlapped merely by a thin pulmonary covering. These murmurs are therefore heard most distinctly over the area of superficial cardiac dulness and over the sternum, and they may frequently be felt there.

Pericardial rubs depend in most cases upon inflammatory deposits. They may come quickly, change their character quickly, and disappear quickly. Their disappearance may depend—(*a*) upon the retrogression of the inflammation; (*b*) upon the formation of adhesions, or (*c*) upon the collection of a fluid exudate, which separates the pericardial layers from each other. A pericardial rub may, however, persist despite the presence of an effusion, for the fluid may be mostly collected in the lateral parts of the pericardium and against the great vessels, and leave enough of the rough visceral layer exposed anteriorly to grate upon the parietal pericardium. Again, even with large exudations, audible rubs may arise from the inferior pericardium if the weight of the

heart have displaced the fluid and brought the two roughened layers in contact inferiorly.

The most trustworthy signs to distinguish pericardial rubs from endocardial murmurs are: the acoustic peculiarity of the former, their decided variability, and their lack of correspondence to the cardiac phases. Pressure of the stethoscope intensifies a rub, but does not affect a murmur. Bending forward from a sitting posture in bed will accentuate a pericardial friction sound, whereas a more decided change of position is required to affect an endocardial murmur. (See p. 388 et seq.) Pericardial murmurs can be influenced by the breathing in as many ways as endocardial. Besides the change of the pressure or pull acting from the outside upon the pericardium, there must be considered the influence of breathing upon the filling and, therefore, upon the size of the heart, and the influence of the pulmonary overlapping of the heart, which varies with each phase of respiration. These are in a measure opposed. Considering the complexity of these relations, it would be hard to find any certain evidence for differentiating between endocardial and pericardial murmurs. But Valsalva's experiment may sometimes be used in making this differentiation. This experiment is performed in the following way: After a deep inspiration the patient attempts an expiration with a closed glottis, and at the same

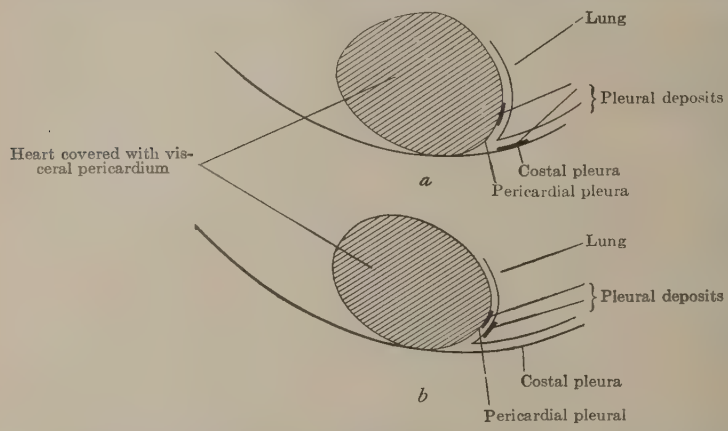


Fig. 161.—Two possibilities in pleuropericardial rubs. Diagrammatic horizontal section of the chest.

time exerts strong abdominal pressure. This maneuver raises the intrathoracic pressure and prevents the entrance of the blood into the heart from the great veins. The test is not suitable for very sick people. As a result, endocardial murmurs after a few pulse-beats grow fainter and often disappear, whereas pericardial murmurs are ordinarily increased, because the inflated lung presses strongly against the pericardium. Faint pericardial murmurs are not transmitted so well as are endocardial of the same intensity, because the latter are not only conveyed by the blood-current, but arise from each of the heart chambers bounding the lesion. Loud pericardial murmurs can, however, be heard over the entire precordia. Finally, all the other signs of pericarditis, on the one hand, and of endocarditis, on the other, should in doubtful cases be utilized to clear up the diagnosis.

Pleuropericardial Rub (Extrapericardial; Pseudopericardial).—Pericardial may be confused with pleural rubs when the latter arise near the heart, because friction of pleura costalis or pulmonalis, on the one hand, and pleura pericardiaca, on the other, may be brought out by movements of the heart as well as of the lung. They are called pleuropericardial, extrapericardial, or pseudopericardial rubs. They appear chiefly near the left anterior pulmonary border.

The usual distinction mentioned for differentiating extrapericardial from ordinary pericardial rubs, viz., that the former exhibits a double phase, both cardiac and respiratory, whereas the latter does not, is not entirely conclusive because, as we have seen, pericardial rubs are also affected by respiration. One of the most essential

points in differentiation is that the maximum intensity of true pericardial rubs is in the region of superficial cardiac dulness and over the sternum, whereas the extrapericardial are best heard outside this area; again, the latter possess distinct cardiac and respiratory phases, while the former are less influenced by the respiration than by the heart action. If the deposit be quite circumscribed, holding the breath in extreme inspiration or expiration will decrease or abolish pleuropericardial rubs, but not easily true pericardial rubs. If this diminution or disappearance occur at the end of inspiration, the roughness will be situated upon the pleura pericardiaca, and so separated by the inflated lung edge from the corresponding roughness upon the pleura costalis (Fig. 161, *a*); whereas if at the end of expiration, the roughness will be upon the pleura pericardiaca and pleura pulmonalis, which are then no longer in contact (Fig. 161, *b*). True pericardial rubs are, on the contrary, usually intensified by holding the breath in extreme inspiration, especially if abdominal pressure be exerted (Valsalva's experiment, p. 346); but this is, of course, better appreciated over the superficial cardiac dulness, where the distended lung edge does not overlap the heart.

Precordial Emphysema Murmur.—If, from the rupture of alveoli, air escape along the interstitial pulmonary tissue to the hilum, and from there to the connective tissue of the anterior mediastinum, the superficial cardiac dulness will be diminished, the heart tones weakened, and resonating, crepitating, or metallic noises simulating râles may appear over the heart. They will be synchronous with the cardiac action, not with the respiration, and thus can be distinguished from the râles of interstitial emphysema. (See p. 301.) From the cardiac râles which may be heard over consolidations and cavities in the neighborhood of the heart, they can be differentiated by paying attention to the relations of the cardiac dulness, of the heart tones, and of the respiratory murmur, by the demonstration of signs of a pulmonary emphysema or of an emphysema of the skin, and by the consideration of other accompanying appearances and the history.

Pericardial Splashing.—If the pericardium contain both air and fluid, a characteristic splashing noise arises synchronously with and in consequence of the heart action. It will resemble what we hear by shaking a patient with pneumothorax and sometimes it will be metallic. The heart tones will then be diminished, or, by the resonance, sometimes increased (pp. 316 and 317), and in the latter event will present a metallic character. The cardiac dulness disappears in the recumbent posture, whereas in the sitting position the fluid pushes the deeper portion of the heart forward and occasions dulness. The heart action may produce similar splashing when there is a distended stomach, large cavities, or a pyopneumothorax, so that we must note the spots where the murmur is most intensely heard, the severe signs of pericarditis or pericardial perforation, the relations of the cardiac dulness, the exact conditions of the lungs, and the modifications, if any, produced by emptying and filling the stomach.

AUSCULTATION OF THE VESSELS

Both tones and murmurs can be heard over the vessels as well as over the heart. (See pp. 326 and 306 et seq. and p. 327 et seq. in regard to the definition of tones and murmurs and the discussion of their origin.) Some of them are transmitted from the heart. The stethoscope is always used to auscultate the vessels, and care should be taken to avoid any pressure.

AUSCULTATION OF THE ARTERIES

The *carotid* is auscultated at the angle of the jaw or at the inner edge of the sternocleidomastoid; the *subclavian*, above the clavicle, between it and the sternocleidomastoid, or below the clavicle, in the so-called "Mohrenheim's fossa," between the pectoralis major and the deltoid; the *brachial*, at the inner edge of the biceps, or at the bend of the elbow with a slightly extended arm; the *radial*, at the place where one ordinarily feels the pulse; the *femoral*, just below Poupart's ligament. Before auscultation the position of the artery should be determined by palpation.

NORMAL CONDITIONS

Two tones are heard normally over the carotid and subclavian—a systolic, from the systolic tension of the vessel-walls, and a diastolic, transmitted from the aortic valves. Over the femoral and over the abdominal aorta we normally hear either nothing at all or a systolic tone. The small arteries are normally toneless.

A so-called "pressure murmur" can be produced by applying a stethoscope with some force upon the larger and even upon the smaller arteries, such as the brachial. This is frequently a very loud, hissing, systolic murmur, and is due to the artificial stenosis of the artery. (See Auscultation of the Heart, p. 327.) If strong enough pressure be applied to occlude the lumen of the artery, a systolic "pressure tone" is produced. Pressure tones and pressure murmurs are perfectly physiologic, so that, to bring out pathologic tones or murmurs, with the exception of Duroziez's double murmur, we should never employ pressure of the stethoscope in auscultating the vessels. A systolic murmur is sometimes heard over the skull of children from the third month to the sixth year, perhaps best over the vertex; it probably arises in the internal carotid,—exactly how we do not know,—is normal and without diagnostic importance. [Fisher called attention to it in rickets.—Ed.]

PATHOLOGIC CONDITIONS

The diastolic, and still more the systolic, murmurs of aortic lesions are readily transmitted to the vessels of the neck. When the second aortic tone disappears in aortic insufficiency, ordinarily but one systolic tone can be heard over the neck vessels.

A systolic tone may be appreciated even over toneless arteries with a pulsus celer of fever or of aortic insufficiency; and with the latter a tone may be appreciated over very small arteries, *e. g.*, the radial [and the dorsalis pedis.—Ed.].

A rarer phenomenon is the double tone over the femoral artery, heard most frequently in aortic insufficiency. Traube has explained this by the fact that in a marked pulsus celer, the systolic tension and the diastolic relaxation of the artery each give a tone. But this is not applicable to the double femoral tone in tricuspid insufficiency, when one, at least, of the tones may be of venous origin. It has even been suggested that in this case they are both due to the venous pulse, one during the contraction of the auricle, the other, of the ventricle. But the auricle is too far away from the femoral vein for such an explanation to seem very probable. In a case reported by W. Schulz[1] from Minkowski's clinic, with both aortic and tricuspid insufficiency, the first tone was shown to be due to the ventricular pulse of the femoral vein, the second to the pulse of the femoral artery, so that the first was caused by the tricuspid, the second by the aortic, insufficiency. The venous tone was, therefore, hastened in comparison with the arterial, as the ventricular venous pulse occurs during closure time, the arterial, not until after its close. The double femoral tone has been noted, though very rarely, in chlorosis, pregnancy, and chronic lead-poisoning. So far no satisfactory explanation for it in these cases has been given.

The so-called Duroziez's double murmur is more common in aortic insufficiency than the double femoral tone. If the pressure of the stethoscope over the femoral or brachial artery be gradually increased, the following series of sounds can be heard: without pressure the single or double arterial tone; with somewhat stronger pressure, the normal systolic pressure murmur; with a further very carefully adjusted amount of pressure, the systolic murmur, followed by a second, generally much fainter, diastolic murmur; finally, with still more pressure, a single or double tone again. This second, diastolic murmur is caused by the diastolic reflux of blood through the artificial stenosis of the femoral. Aortic aneurysm will sometimes furnish this double murmur if there should be a diastolic reflux of blood into the sac. It may also be found with any pulsus celer, *e. g.*, in chlorosis and exophthalmic goiter. The author has heard it over the left lobe of the liver in a case of inflammatory arterial liver pulse (see p. 198) by applying strong pressure with the stethoscope. A good deal of patience is required for the demonstration of the Duroziez phenomenon, because it is a question of applying just the proper amount of pressure.

A systolic murmur heard only over one subclavian artery, when the arm is hanging down and when no pressure is exerted by the stethoscope, suggests chronic disease of the apex of the corresponding lung. Pleural adhesions to the subclavian vessel sheath probably twist the artery, and so cause the murmur. Inspiration applies the thorax more closely against the stethoscope, so that we must be careful

[1] W. Schulz, Deut. med. Woch., 1905, vol. xxxv.

to avoid any pressure. Sometimes, however, a subclavian murmur can be heard on both sides, more rarely on one side, in perfectly healthy people, and in many persons such a murmur may also be caused artificially by certain positions of the arms which compress the artery against the clavicle or against the subclavian and pectoralis minor muscles.

Systolic murmurs heard over the arteries, especially the carotids, without stethoscopic pressure, possess some diagnostic interest. They may arise in anemia in the same way as accidental heart murmurs (p. 340), and if not transmitted from the heart, they are often of the greatest importance in verifying the accidental character of a heart murmur in the same way as the venous hum (p. 349). The increase of the systolic blood-stream in the pulsus celer of aortic insufficiency, exophthalmic goiter, and chlorosis can cause murmurs over the arteries, independent of any transmission.

Localized arteriosclerosis will furnish a systolic murmur over an artery. A case of this kind was of considerable interest to the author. An old man presented a loud systolic murmur over the left carotid for months, and the diagnosis of an arteriosclerosis of that carotid was confirmed later by the onset of a left-sided cerebral thrombosis. Slight pressure of the stethoscope—not enough to cause a murmur in a normal artery—will sometimes bring out such an arteriosclerotic murmur. Litten recently emphasized its diagnostic importance, and described it as a phenomenon of palpation, under the name spurts—"Spritzen." It may be heard over the abdominal aorta as well as over the carotids.

Systolic and diastolic murmurs are frequently heard over *the enlarged thyroid* of exophthalmic goiter. The systolic are doubtless arterial, dependent upon a pulsus celer. It has not been determined whether the diastolic are arterial, and, like the second part of the Duroziez double murmur, a consequence of pulsus celer (in which case they are heard only with a certain pressure of the stethoscope); or whether they are the diastolic portion of venous murmurs (p. 350), isolated and strengthened because the veins are compressed or closed by the arteries during systole.

Any one who takes the trouble to auscultate the vessels frequently will hear sounds which have never been described and many which have not been thoroughly explained. The author mentions as an example the occurrence of three sounds in the carotid in cases of aortic insufficiency, which together give a rhythm completely analogous to the gallop rhythm of the heart, although such a rhythm is not present in that organ. It is probably produced by a combination of the transmitted first sound of the heart (intracardiac tension tone) with the two normal carotid tones, or by an arterial double tone with a transmitted diastolic tone from the aortic valve. In aortic insufficiency the author has also repeatedly heard a presystolic murmur, *i. e.*, presystolic in reference to the local arterial sounds, which is probably produced by the marked increase in the velocity of the current (pulsus celer) preceding the systolic distention of the artery.

AUSCULTATION OF THE VEINS

TONES OVER THE VEINS

The blood flows through the veins normally without tones and without murmurs. The so-called venous hum is only very rarely heard in healthy individuals. The reflux blood-wave of the venous pulse in the greater veins (especially in the jugular vein and in the bulb) may cause a systolic tone, due to the relaxation of the valves and of the walls of the vein. This is particularly the case where the venous pulse is due to the strong pressure during regurgitation in a tricuspid insufficiency. In this case the valve tone over the bulb slightly precedes the systolic carotid tone. (See p. 199.)

For the so-called double venous tone over the femoral see p. 348.

MURMURS OVER THE VEINS; VENOUS HUM

Most venous murmurs are continuous, because the current in the veins varies so little in rapidity. The most important is the so-called

"venous hum," "nun's murmur," or "bruit du diable." It is heard over the jugular vein very frequently in anemic and chlorotic individuals, and not infrequently in health. It exhibits a characteristic continuous sound, sometimes blowing, sometimes humming, and sometimes musically whistling, with a rhythmic accentuation corresponding to systole, to diastole, and to the phase of respiration. It is heard most plainly on the right side, over the carotid, in the angle between the sternum and the clavicular portion of the sternocleidomastoid. The patient should stand erect and hold his head straight, because the recumbent posture diminishes the intensity of the murmur and sometimes causes it to disappear. Turning the head to the opposite side ordinarily increases the murmur. Pressure of the stethoscope should be avoided, for if marked pressure be exerted, the murmur practically always disappears, and then the carotid tone or an artificial murmur of the stenosed carotid is all that is heard. If faint, we can sometimes distinguish only the accentuated systolic, diastolic, and inspiratory portions of the venous hum. Such an interrupted murmur may be confused with an arterial or with a respiratory murmur. Pressing very lightly with the stethoscope or turning the patient's head toward the opposite side will, however, intensify the hum and transform the interrupted murmur into a continuous roar, and so clear up the diagnosis. The diastolic accentuation of a venous hum may be transmitted to the cardiac region and simulate a diastolic accidental murmur, but auscultating from the heart to the jugular will generally distinguish the one from the other (p. 342).

To explain the venous hum we must start with the fact that it occurs, although not exclusively, yet much the most commonly, in anemic individuals; and then we must turn to the general physical laws applying to the origin of murmurs in flowing currents (p. 328 et seq.). The two factors which are all important in producing current murmurs are: (1) the presence of abnormal narrowings or widenings in the tube, and (2) the current rapidity. To explain the venous hum in anemic individuals the hypothesis has been advanced that the jugular veins collapse in consequence of a diminished mass of blood, whereas the *bulbus* remains distended in virtue of its attachment to the cervical fascia. An abnormally pronounced change of lumen thus results between the vein and the bulb, and so produces the murmur. This explanation is certainly incorrect, because, in the first place, in those anemic individuals in whom the venous hum is most common (chlorotics), the supposition of a diminished blood-mass is quite erroneous, and because, in the second place, it is easy to see that in chlorosis the jugular veins are generally well filled, and indeed often abnormally so. Since we must give up the hypothesis of a change of lumen at the auscultation spot of the jugular vein as an explanation of the murmur, we must turn our attention to the second of the above-named factors, viz., the current rapidity. Have we any proof that anemic blood flows with increased rapidity? Cohnheim's experiment in submitting the mesentery of an artificially hydremic animal to direct observation proved that hydremic blood actually flows more quickly than normal blood, and probably on account of its diminished cohesion or viscosity.[1] Though anemic individuals usually exhibit a diminution of the blood-coloring matter, their blood is not necessarily hydremic. Nevertheless, specific gravity estimations of their blood do show that it is very frequently hydremic;

[1] Allg. Path., 1882, vol. i, p. 441.

and, besides, it is perfectly conceivable that the cohesion or viscosity of anemic blood is diminished even without actual hydremia, and so the friction between the layer of blood against the vessel-wall and the circulating current would be diminished, and hence result in an increase of the current rapidity.[1] An increased current rapidity would naturally offset to some extent the disadvantage of a deficient hemoglobin. The explanation that the venous hum in anemic individuals depends upon an increased rapidity of the current is certainly the most probable. Of course, this theory assumes a normal change in lumen between the jugular vein and the bulbus. The venous hum which is quite rarely observed in perfectly healthy individuals may reasonably be supposed to depend upon individual anatomic relations or conditions of distention of the vein sufficient to narrow its lumen and produce a murmur with normal current rapidity. The current rapidity of the blood may perhaps also vary within normal limits sufficiently to explain the venous hum in healthy individuals.

We explain the accentuation of the hum in the standing position by the influence of gravity upon the column of venous blood: it exercises suction, thereby narrows the vein, and so hastens the jugular blood-stream. The murmur is more plainly heard upon the right side, because the right jugular vein is almost a direct linear continuation of the right innominate vein; whereas the left jugular empties into the left innominate at an oblique angle, and so there is less obstacle to the current on the right side. By turning the head to the opposite side, the upper part of the vein is compressed by the sternocleidomastoid and omohyoid, hence this movement accentuates the venous hum. The accentuation due to the stethoscopic pressure needs no further explanation.

The rhythmic accentuation of the hum requires explanation. The inspiratory intensification is easily explained by the increased rapidity of the venous blood during inspiration. The explanation of the systolic and diastolic accentuation may be understood from an examination of the curve of the physiologic venous pulse (Fig. 109) or of the normal auricular pressure (Fig. 111), in which the two depressions x and y (x corresponding to systole of the ventricle, y to diastole) indicate an increase of rapidity in the venous blood-current.

Murmurs similar in character and origin to the venous hum may also be heard over the femoral vein and over a vascular goiter. In the latter they may be favored by irregularity of the lumen of the blood-vessels and the tortuosity of the veins.

The author attributes considerable diagnostic significance to the presence of a venous hum. If not absolutely pathognomonic, it at least, in suspected cases, suggests the presence of anemia. The demonstration of a venous hum confirms the diagnosis of an accidental heart murmur. A venous hum is also found in exophthalmic goiter, and is located most frequently over the goiter. Here, too, it probably depends upon an increased rapidity of blood-current.

[1] This theory is supported by the few investigations so far made concerning the viscosity of the blood.

AUSCULTATION OF THE ABDOMEN

Excepting for the sounds heard over the pregnant uterus (fetal heart tones,[1] uterine and placental bruits and cord murmurs), described in text-books on obstetrics, auscultation of the abdomen is generally barren of results. (Compare the section upon Auscultation of the Vessels (p. 347 et seq.) in regard to the examination of the abdominal aorta.) Friction murmurs synchronous with respiration, caused by peritoneal exudations over the liver or spleen (ordinarily palpable as well), have a certain importance (perihepatitic and perisplenic friction murmurs). Gerhardt claims that cases of cholelithiasis very frequently furnish such friction sounds in the region of the gall-bladder. Similar friction murmurs arise over other parts of the abdomen between roughened surfaces of the peritoneum, but they are generally better appreciated by palpation than by auscultation, because they are best brought out by manipulation. In normal cases intestinal movements proceed so quietly that only very faint intestinal murmurs are to be heard; but in pathologic increase of peristalsis the intestinal movements can sometimes be heard at a distance—the so-called "borborygmi." Further, the coincident presence of gas and fluid in the abdominal cavity may, in moving a patient with perforative peritonitis, cause succussion murmurs in the abdomen, frequently metallic in character and similar to the *succussio Hippocratis* (p. 301). They may be sometimes heard by means of the stethoscope, occasionally at a distance. They possess a certain interest but no great diagnostic significance, since in the very diseases whose differentiation from perforative peritonitis is desired (for example, in ileus and in non-perforative peritonitis), there is ordinarily an accumulation of air and fluid in the stomach and distended intestines capable of giving rise to the same sort of a succussion murmur. The so-called "splashing noise" will be mentioned under Palpation of the Abdomen. In the diagnosis of intestinal stenosis (from tumors) the author has several times been aided by the presence of a hissing or whistling stenotic murmur, appreciable sometimes at a distance even by the patient himself, sometimes by means of a stethoscope, and sometimes by palpation. This is due to peristalsis, gas and fluid being forced through a stenosis in the intestines. A peristaltic wave or a colicky pain will point to the best time for examination. (See Auscultatory Percussion of the Abdomen, p. 257 et seq.)

Auscultation of the Esophagus.—(See the section, Examination of the Esophagus.)

PALPATION OF THE LUNGS AND PLEURA

(In regard to the inspection of these parts see the section, Character of Respiration, p. 84 et seq.)

As has already been mentioned in several places (Râles, Rubs, Succussion Murmurs), palpation of the lungs and of the pleura serves partly to confirm symptoms recognized by auscultation, partly to furnish independent results. Examining for fluctuation, changes of resistance of the thorax, abnormal pulsations and pectoral (tactile) fremitus belong to the special province of palpation.

[1] The fetal heart tones are usually considered not to be audible before the middle of pregnancy, but Sarwey has shown that they may be regularly heard from the thirteenth week, over a circumscribed deep area of the anterior wall of the uterus. To appreciate them, the bladder must be emptied, the room be kept absolutely quiet, and the examiner be possessed of normal hearing and exercise the greatest patience.

DETERMINATION OF FLUCTUATION AND CHANGES OF RESISTANCE IN THE THORAX

Fluctuation is obtained over superficial accumulations of pus or over a purulent exudate which has broken through the chest-wall and lies directly under the skin (a so-called *empyema necessitatis*). No real fluctuation can ever be appreciated over a serous or non-perforating purulent pleurisy because of the tension of the soft parts between the ribs.

But a kind of fluctuation or thrill (vibratory fluctuation) can be obtained over an effusion which extends from the front to the back of the thoracic cavity, by vigorously percussing the posterior thorax, and at the same time, with the other hand, palpating the front of the corresponding half of the thorax (bimanual palpation percussion). The appreciation of this phenomenon requires a very nice sense of touch. The author has noticed it in exceptional cases of sero- and pyopneumothorax, where the free mobility of the fluid permits a strong vibration wave. Here the phenomenon has some diagnostic importance, because the fluid lying beneath the lung cannot be demonstrated by percussion until it has reached a certain volume. (See p. 269.) The succussion felt in sero- and pyopneumothorax is an accentuation of the same phenomenon.

Palpation over pleuritic exudates and the different kinds of lung consolidations ordinarily detects an increase of resistance, which frequently the finger as plexor also appreciates during percussion.

ABNORMAL PULSATIONS IN THE REGION OF THE LUNGS AND PLEURA

Pulsation over the precordia will be described later (p. 355 et seq.). Where pulsating tumors have pushed the lungs aside and lie against the thorax, inspection or palpation, or both, may appreciate such pulsation over the chest. In marked mitral lesions, especially insufficiency, one can palpate, here and there through the thoracic wall, diffuse pulsations of the lungs. This can be appreciated better with the ear applied to a rigid stethoscope against the chest than with the hand. (See p. 356.) The phenomenon, due to an increased pulse in the pulmonary vessels, must be distinguished by its diffuse character from a mere mechanical heaving of the thorax transmitted from the heart. A pulmonary pulse may also be detected in insufficiency of the pulmonary valves (pulsus celer of the pulmonary artery). Pleural exudates may pulsate in the intercostal spaces (pulsating pleurisy) by transmitting the heart movements through the fluid to the intercostal spaces. This phenomenon is very rare, because the tension of the soft parts between the ribs is too great unless they and the pleura itself become softened and decomposed from the inflammation, and unless the intrapleuritic tension is diminished to equal that of the atmosphere. In short, empyemas, but only very few serous exudations, pulsate.

TESTING THE VOCAL (TACTILE) FREMITUS

By vocal (tactile) fremitus is meant the purring vibration appreciated by the hand placed upon the thorax of a person speaking or singing. It arises from the transmission of the vibrations of the glottis through the air in the trachea and bronchi to the thoracic wall. Physiologically, the louder and deeper the voice, the stronger the fremitus. The fremitus frequently cannot be appreciated in women with high voices, in very fat people, and in patients too sick to speak aloud. In children it is less distinct than in adults, and is often absent. The fremitus is strongest at the upper posterior parts of the thorax, over the great bronchi. From there downward and outward it is gradually diminished.

The fremitus is caused by the vibrations of the lungs and thorax set in motion by the transmitted vibrations from the glottis during speaking. What is felt then, is the vibrations of the deep pulmonary tones demonstrated by Sellig in his experi-

ments on the percussion-note. That the fremitus is most distinct with a man's voice is due, not only to the fact that the slow vibrations of a deep voice can be better felt, but also to the fact that these slow vibrations harmonize with those of the deep pulmonary note, and, therefore, can easily evoke them, while the rapid vibrations of a woman's voice can not. In a child, although the vibrations of the glottis are rapid, the pulmonary tone is also high, so that the harmony is better than in a woman.

Differences in the fremitus over different places of the thorax are appreciated by comparative palpation while the patient speaks the same words aloud; for example, "one, two, three," or "ninety-nine." The ulnar edge of the hand, which is generally endowed with a very keen sense of touch, appreciates the fremitus most accurately. The naked ear applied to the thorax will serve the double purpose of auscultation and palpation. Naturally, we should compare only symmetric parts, and we should remember that the fremitus is normally somewhat stronger upon the right than upon the left side, on account of the greater width and the more direct branching of the right bronchus. [Fetterolf,[1] in a very convincing anatomic study, explains this difference more simply. He states that the vocal vibrations are transmitted directly from the trachea through the tissues of the superior mediastinum to the lung apices. The trachea is about 10 cm. long, with approximately three-fifths of its length in the thorax. On its right side almost entirely throughout its thoracic course the lung lies in contact with it, separated only by the parietal pleura and a delicate layer of areolar and lymphatic tissue. On the left side there are 3 cm. or more of large blood-vessels and esophagus plus areolar and lymphatic tissue interposed between the trachea and the apex.—Ed.]

Similar rules apply to the increase and decrease of the fremitus as to the voice itself and of the physiologic laryngotracheal breathing murmur. The fremitus is increased wherever bronchophony appears (p. 302 et seq.), *i. e.*, over infiltrations and other consolidations of the pulmonary parenchyma so long as the bronchi remain patent, over cavities and over dilated bronchi. It is diminished if the bronchi be plugged, or if gases, fluid, or solid tissues intervene between the pulmonary surface and the chest-wall (pneumothorax, pleural exudates, tumors). Increased fremitus corresponds, as a rule, to bronchial breathing and to bronchophony; diminished fremitus, to diminished breathing and lack of bronchophony. Yet frequently in one and the same case there are factors working at variance with one another for the production of bronchial breathing, bronchophony, and increased fremitus. Such factors do not always affect them equally. So, although these three signs are of the same diagnostic import, we must determine each one separately. For example, in pleuritic effusions the exudate decreases while the pulmonary compression increases bronchophony, bronchial breathing, and fremitus; but the effect upon each of these signs is not the same, for frequently over a moderate-sized pleural exudate we get bronchial breathing and bronchophony, but diminished fremitus.

Fremitus is always increased over pulmonary consolidations except when the bronchus leading to the consolidated part is occluded by secretion, by a foreign body, or by a compressing tumor. It is then absent or decidedly diminished, although usually not permanently, as the secretion, which is the usual source of the plugging, may be coughed up.

The rule that the fremitus is diminished over fluid exudations and

[1] Arch. of Int. Med., February 15, 1909, vol. iii, No. 1, p. 23.

over pneumothorax also has exceptions, because if the exudate be small, the compressed lung increases the fremitus more than the exudate diminishes it. This is rare; but increased fremitus as well as bronchial breathing is common at the upper border of the pleuritic exudate, where the fluid layer is thin and wedge-shaped (see Fig. 145, I), whereas toward the base it is plainly weakened. (See Fig. 147, I.) Finally adhesions, if membranous or string-like, can transmit the fremitus to the surface through an exudate or through a pneumothorax.

One of the helpful methods of determining the level of the fluid in a pleuritic exudate is to map out accurately the line of demarcation between this increased and decreased fremitus. In tapping a chest we may sometimes avoid circumscribed adhesions within the area of a pleuritic effusion or of a pneumothorax by testing the fremitus.

Changes in the thoracic wall also influence the fremitus. Thickening of the wall, edema, and the like, diminish it. Over differently curved portions it varies under otherwise equal conditions, so that the relations of fremitus are not trustworthy in the scoliotic or deformed chest. Changes of elasticity of the thorax decidedly influence the fremitus, so that it may be diminished over contracted portions after pleurisy, even without any exudate or any considerable thickening of the pleura.

INSPECTION AND PALPATION OF THE HEART REGION (PRECORDIA)

We shall discuss these two methods of examination together, because they are so intimately related. Marked bulgings of the heart and of the pericardium have already been described in the section upon the Shape of the Thorax (p. 30).

HEART-BEAT AND APEX-BEAT

The heart-beat is the visible and palpable impact of the heart against the thorax; the heart apex-beat, more simply apex-beat, the portion confined to the neighborhood of the apex. Most diagnostic points are especially concerned with the apex-beat. To locate the heart-beat correctly, place the flat of the hand upon the precordia horizontally and close to the left parasternal line, with the fingers reaching to the left axillary line. The finger-tips may, at the same time, be utilized for more accurate localization of the apex-beat. If the examiner stand in front of the patient, he uses his right hand; if he stand behind the patient, the left hand. In women with large breasts the entire left mamma must be drawn up to the right. *Sp.* designates the apex-beat in our diagrams.

As Laënnec pointed out, the heart-beat can generally be appreciated better with the ear applied to the end of a rigid stethoscope than with the hand. As the skin of the ear is certainly not so sensitive to touch as that of the hand, this must be due to the vibrations of the rigid tube of the stethoscope caused by the heart-beat. This advantage can also often be gained if the hand, instead of the ear, be applied to the stethoscope. In ordinary palpation the contact of the two soft surfaces tends to dull

the vibrations. It is often advantageous, when auscultating the heart, also to use the ear for this method of palpation. The author has often been able to demonstrate by this "palpatory auscultation" a dilatation of the heart to the right or left which his students could not make out in any other way. Von Kürl[1] makes use of this principle in his "indirect palpation," employing a special instrument for the purpose, which he calls the "ictometer."

HEART-BEAT UNDER NORMAL CONDITIONS

An impulse synchronous with the heart action, and for the most part systolic in time, can be felt over the precordia of healthy individuals. This is called the heart-beat, and with it a slight systolic depression to the right and above the apex can sometimes be felt. The actual apex-beat is limited to a circumscribed area (one or two neighboring intercostal spaces). It may be visible or palpable, one or both. Its middle point either corresponds accurately to the apex of the heart, *i. e.*, to that point of the deep cardiac dulness which lies farthest to the left, or, more often, lies a little within this point. The latter position, under normal conditions, seems to be due to the fact that the outer part of the apex-beat is dulled by the overlapping lung, so that the maximum beat is appreciated a little within the true position of the apex. (See p. 232.) Under pathologic conditions, various other causes may be responsible for this. (See p. 360.) For positions of the apex-beat outside the orthodiagraphic heart projection, see p. 233.

In adults the apex-beat lies normally in the fifth intercostal space, somewhat inside of the mammillary or midclavicular line. In children it may be situated a space higher; in the aged, a space lower. Even in adult life its position depends a good deal upon the form of the thorax; variations of about one intercostal space may be within physiologic limits. In small children the apex-beat may lie physiologically somewhat beyond the midclavicular line. The extent of the apex-beat varies; ordinarily it covers an area about 2 cm. square. In conformity with the results of topographic percussion, the heart apex, during median respiration, is generally covered only by a thin layer of lung, which cannot interfere with the appreciation of the apex-beat, but which may sometimes cause, as has just been said, the dislocation inward of its maximum point. Still, the heart apex may normally lie directly against the thoracic wall and so render the apex-beat more distinct. Under pathologic conditions, the enlarged right ventricle, more or less spread out, may share in the production of the apex-beat, although normally, as is well known, the heart apex is formed by the left ventricle alone.

The intensity of the apex-beat varies a great deal even under physiologic conditions, depending upon the amount of overlapping lung and upon the thickness and resistance of the thoracic wall. These variations and the fact that the apex may lie behind a rib instead of opposite an intercostal space make it clear why quite healthy persons sometimes show no distinct apex-beat. Normal breathing does not alter the position or the intensity of the apex-beat, but a deep inspiration generally hides it. Inspiration may depress it, due to the respiratory descent of the diaphragm and of the heart; expiration elevates it.

In accordance with the passive alteration of the position of the heart described under Topographic Percussion (p. 229 et seq.), the apex-

[1] Wien. klin. therap. Woch., 1904, vol. xxi–xxiv, and Wien. klin. Woch., 1905, vol. xiv.

beat can change its position, moving to the left in left-sided positions, to the right in right-sided positions,[1] of the body or in the latter being completely obliterated by the overlying left lung. Bending the trunk forward in the erect posture, and so pushing the left lung edge somewhat aside, frequently brings out the apex-beat more plainly. This device is to be recommended in attempting to localize the left heart boundary when the apex-beat is rather indefinite. Of course, any lateral movement of the trunk should be avoided. Similarly, deep expiration will sometimes bring out the apex-beat, because the lung is thus more completely retracted. The Valsalva experiment, combining expiration with abdominal pressure, is not applicable, because it hinders the flow of venous blood to the heart, and so diminishes its size.

Stimulation to cardiac activity, either psychic stimulation or bodily exertion, intensifies and diffuses the apex-beat.

According to physiologists, the essential cause of the heart-beat is a projection of the heart apex and the neighboring portions of the anterior ventricular wall against the thoracic wall. Such projection is caused by the systolic change in the heart's shape. Martius' experiments demonstrated that the entire phenomenon of the heart-beat occurs within the systolic "closure time" when no blood has yet left the ventricle, but still remains there under higher tension. These experiments refuted all the other theories (recoil theory, theory of systolic stretching of the vessels). Under pathologic conditions certain other factors besides the change of form of the anterior ventricular wall must have some influence in the causation of circumscribed or diffuse pulsations over the precordia. (See p. 366 et seq.)

PATHOLOGIC DISLOCATION OF THE HEART-BEAT

The heart-beat may be displaced by an enlargement of the heart or by its dislocation.

The Heart-beat Influenced by Alterations in the Size of the Heart.—The left ventricle normally gives rise to the heart-beat; dilatation of its cavity in particular will, therefore, displace the apex-beat to the left, sometimes even out to the left axillary line. Dilatation of the right ventricle may also cause a marked displacement of the apex-beat to the left. (See p. 242.) Therefore we have no right to assume that a dilatation is limited to the left ventricle, because the apex-beat is displaced to the left, without paying special attention to all the other pathologic signs. If such a displacement be very marked, and if at the same time there be no increase of cardiac dulness to the right, we are justified in assuming a preponderating dilatation of the left ventricle. The heart apex rests closely against the surface of the diaphragm, running obliquely downward and to the left, so that in dilatation of the left ventricle an apex-beat pushed to the left will also usually be situated lower than normally. Dilatation of the right ventricle, on the contrary, merely dislocates the apex horizontally to the left, because an enlargement of the right ventricle, supported upon the diaphragm, tends to raise the heart apex. (See Fig. 120.) The dome of the diaphragm must necessarily follow this elevation under the influence of the air pressure from the abdomen. It is, nevertheless, doubtful if this distinction always ap-

[1] Wien. klin. therap. Woch., 1904, vol. xxi–xxiv, and Wien. klin. Woch., 1905, vol. xiv.

plies, because with marked dilatation of its chamber the right ventricle forms the apex itself, which must then drop downward in the direction of the heart's axis.

Simple hypertrophy of the cardiac muscle without dilatation is hardly ever sufficiently marked to occasion any noticeable dislocation of the apex-beat. (See p. 243 for exceptions to this statement.)

Only the most marked degrees of cardiac atrophy would be accompanied by or associated with a dislocation of the apex inward.

Displacements of the Heart-beat from Dislocation of the Heart.—(See the section upon Topographic Percussion, p. 249 et seq.)

In *situs inversus* the apex-beat occupies the corresponding point upon the opposite side. In *deformities of the thorax* the apex-beat may be displaced in any direction. In *emphysema* it lies lower than normally, although often the heart is so thoroughly covered by the lung that it cannot be felt at all. In *unilateral retraction* of the lung the apex-beat may be drawn toward the affected side and generally upward, the latter on account of the high position of the diaphragm. *Pleuritic exudates and pneumothorax* cause a purely lateral dislocation of the apex-beat. (See p. 250.) If the dislocation be excessive, there may be added a pendulum movement. If a left-sided effusion or pneumothorax extend around in front of the heart, the apex-beat may disappear. Right-sided effusions will sometimes crowd the apex-beat almost to the left axillary line, and frequently to an abnormal height, in consequence of a rotation or pendulum movement, the left side of the diaphragm, of course, accompanying the apex. *Retraction of the left lung* and consequent dislocation of the mediastinum will accomplish a similar result. Increase *of the intra-abdominal pressure* from *meteorism, ascites, tumors,* etc., will force the apex-beat upward, and frequently, in consequence of a pendulum movement, somewhat to the left. (See p. 249 et seq.)

INTENSIFICATION AND DIFFUSION OF THE HEART-BEAT

We appreciate the intensity of the apex-beat both by inspection and palpation. If the palpating finger be raised quite vigorously, the apex-beat is characterized as forcible or powerful. Under such circumstances it is often diffused, shaking the entire precordia, although the actual apex-beat can almost always be determined by localizing a circumscribed area of more decided elevation. Such a strong movement signifies nothing but an intensification of the apex-beat of no very exact import, because the strength of the beat varies so decidedly, even under physiologic conditions.

The apex-beat is increased pathologically (and then ordinarily also diffused) by any *stimulated condition of heart action* (*bodily exertion, nervous palpitation, exophthalmic goiter, acute and chronic tobacco-poisoning, fever*). Cardiac dilatation, even without any pronounced hypertrophy or increased cardiac activity, not only displaces and diffuses the apex-beat, but also intensifies it. This seems anomalous; and so does the violent heart-beat with weakened pulse which is so often observed in uncompensated heart lesions and in the so-called overexertion of the heart. But Martius' cardiographic experiments proved that the heart-beat occurs during the closure time of systole, and that it is entirely independent of the power with which the ventricle empties its contents. The larger

the heart, the greater the change of its form at the closure time, and consequently the more marked the heart-beat, quite independent of the heart's power. In conditions of cardiac weakness the closure time is prolonged at the expense of the expulsion time; the heart only moderately diminishes during diastole; the heart-wall during the expulsion time moves from the thoracic wall only a little and quite slowly, and so the change of form during closure time is emphasized, and the heart-beat seems especially strong. Conversely, it is plain that when the heart's power improves in such a case the heart-beat will become weaker, because the expulsion of the blood begins earlier, is more complete, the heart becomes smaller more quickly during systole, and therefore recedes farther from the thoracic wall.

An accentuation and diffusion of the heart-beat frequently signifies merely a more extensive uncovering of the heart (pulmonary retraction, high position of the diaphragm, upward dislocation of the heart). (See p. 251.)

As has been said, an abnormally powerful apex-beat alone does not always signify cardiac hypertrophy. But one form of increased apex-beat, F. Müller's[1] so-called "heaving beat" (or, better, in the author's opinion, "slowly heaving apex-beat") admits of no doubt; it always implies cardiac hypertrophy. In this, although the heart action need not be violent, and is frequently not especially diffused, yet the heart apex lifts the palpating finger with pressure and with irresistible force. Very frequently also the heart action is slowed. These cases are characterized, according to Müller, by an exceptionally slow elevation of the cardiographic curve and by an increased systolic intracardial pressure, as well as by an increased resistance to systole. The slowness of the heaving depends upon the prolongation of the closure time, whereas the intensification of the heaving is the direct palpatory expression of increased intracardial pressure. The high intracardial pressure, *i. e.*, the resistance to the ventricular contraction, may depend upon a high arterial pressure or upon some opposition to ventricular emptying between the heart and the arteries, *e. g.*, an aortic stenosis. In any case it necessitates a cardiac hypertrophy to overcome the resistance, so that any permanently slow heaving apex-beat may be regarded as a safe sign of cardiac hypertrophy (primary hypertrophy). More importance should be attributed to the slowness of the heaving than to its force and extent, in order to prevent confusion with the increased beat in cardiac insufficiency, just mentioned above. In the recognition of cardiac hypertrophy a slow heaving heart-beat has about the same diagnostic significance as a persisting high-tension pulse.

It is not as yet certain whether other forms of ventricular hypertrophy which depend upon increased diastolic ventricular filling (the so-called secondary hypertrophy (see p. 382, 2) may eventually lead to the slow heaving apex-beat described above, or to a mere accentuation of the apex-beat. Increased resistance, which prolongs the closure time, does not seem to exist in the secondary hypertrophy depending upon dilatation. The effect must, however, be similar, because (according to Pascal's law of the hydraulic press) so long as the arterial pressure remains the same, the total ventricular burden increases in proportion to the inner surface of the ventricle. Future exact palpatory and cardiographic examinations must settle the question whether this kind of "overburdening" can produce the slowly heaving apex-beat, for evidently "overburdening" is not identical with increased arterial resistance.[2]

F. Müller's "vibrating apex-beat" differs both from the simple increased beat and from the slow heaving beat. Its impulse is more rapid and sudden, depending, according to Müller's experiments, upon a change in the form of cardiac stimulation. It is practically confined to subjective cardiac palpitation, especially the nervous form.

It would be of interest to determine whether, as is apparently the case, the di-

[1] Berlin. klin. Woch., 1895, No. 35, p. 757.

[2] O. Frank (Zeit. f. Biol., vol. xxxii) and Moritz (Deut. Arch. f. klin. Med., vol. lxvi) call the burden of the ventricle caused by increased filling "burdening" ("Belastung"); and that caused by arterial resistance or tension, "overburdening." They show that the two factors have an entirely different importance in the heart activity. The original work must be consulted for this distinction.

versity in the apex-beat corresponds to a differing duration of systole. This may be done by employing the method of measuring the duration of systole described on p. 311.

As soon as the major part of the heart is uncovered, the apex-beat is no longer localized; but the entire precordia seems to vibrate with a wave-like movement, an undulation in which the different parts taken by the movement of the ventricles, auricles, and great vessels can often be distinguished. (See p. 367 et seq.)

Compare p. 325 et seq. for the relation of the so-called gallop rhythm to the diastolic recoil of the ventricular walls.

The "dome-shaped" apex-beat in aortic insufficiency should also be mentioned. (See p. 398.)

WEAKENING OF THE HEART-BEAT

The heart-beat may be weakened or may entirely disappear. Either effect may be produced by an *emphysematous lung* overlapping the heart; by *pericardial or left-sided pleural effusions;* by *pneumothorax;* by *tumors* or *collections of air in the anterior mediastinum;* by *marked panniculus adiposus;* by *edema* or *emphysema of the chest-wall.* (See Fig. 17.)

Its disappearance on account of a pericardial effusion is diagnostically the most important of these causes. Before any conclusions can be drawn as to the presence of such an exudate, the character of the apex-beat in health should have been observed, because it may not have been typical before the patient's illness. Pericardial effusions do not always hide the apex-beat. The author once saw a case in which, despite a very large pericardial exudate, the apex-beat persisted, because the apex of the heart was adherent to the parietal layer of the pericardium.

[A case of pneumonia at the City Hospital whose apex-beat was plainly visible and slightly heaving to palpation in the anterior axillary line showed at autopsy a "pericarditis with localized double empyema of the pericardium. The middle and lower portions of the pericardium were adherent to the heart, the upper and right portion over the right auricle was dilated and filled with several ounces of thick greenish pus; on the left side of the heart, and directly over the left ventricle, another sac, somewhat smaller, contained several ounces of similar pus."—Ed.]

Further, as the persistence of the pericardial friction proves, a considerable pericardial effusion may collect and distend the lateral portions of the cavity before it conceals the apex-beat. (See p. 345.)

A weakening or disappearance of the heart-beat is, in exceptional cases, observed as a consequence of diminished *cardiac activity;* but these are mostly conditions of excessive cardiac weakness (agony, collapse). The heart-beat diminishes when the cardiac power becomes so weak that the alteration in shape of the heart during closure time essential to the production of the heart-beat fails. But before this point is reached, the heart-beat will be vigorous or even increased in spite of the diminishing cardiac power.

The diminished tension of the radial pulse is generally a far safer guide to the condition of the cardiac power than a weak heart-beat, especially if we are not familiar with the patient's normal heart-beat.

ABNORMAL POSITION OF THE APEX-BEAT IN RELATION TO THE CARDIAC DULNESS

The apex-beat may lie inside of the cardiac dulness, or, perhaps, more clearly expressed, the deep and sometimes also the superficial cardiac dulness may extend to the left beyond the apex-beat. This

peculiarity may occur in a case of pericarditis, where the exudate is collected in the lateral portions of the sac and the apex-beat still persists, especially if the superficial dulness extend very far to the left of the beat. It is not, however, a pathognomonic sign of such a condition, for the apex-beat may lie within the deep cardiac dulness even under normal conditions (see p. 356), and within the superficial dulness under pathologic conditions other than that of pericarditis, *e. g.*, in mitral insufficiency. In this lesion the apex often belongs partly to the right heart in consequence of the hypertrophy and dilatation of the right ventricle. Again, the same sign may occur in all kinds of cardiac enlargements if an enlarged left ventricle had compressed the lung edge enough to make it atelectatic; the apex-beat would, of course, be further to the left than normal, but part of the increased dulness to the left of the apex-beat would be formed by the compressed lung.

SYSTOLIC RETRACTION AT THE APEX; THE DIASTOLIC "REBOUND" (BRAUER)

This is sometimes observed instead of an apex-beat. It can be shown to be systolic by auscultating the heart.

If noted in a healthy individual, as it sometimes is, the sign cannot be perfectly explained. The author's theory, however, is as follows: The change of form of the heart normally causes a blow of the apex against the chest-wall; at the same time the sections of the heart lying above and within the apex retreat toward the interior of the thorax. Under physiologic conditions this would produce a palpable and visible systolic retraction of the thoracic section lying inside of the apex-beat. (See p. 356.) If, then, for some reason or other the apex-beat be absent, we might be tempted to speak of a systolic retraction of the heart apex; but in reality the apex would not be systolically retracted, but, rather, a part of the anterior cardiac wall lying above and inside it.

In some cases a systolic retraction at the apex or the precordia may be due to an adhesion of the parietal and visceral pericardium, and, generally, an adhesion of the pericardium to the pulmonary and costal pleura.

These cicatricial adhesions hinder the normal change in the shape of the heart during closure time and favor the contraction of the heart in the direction of its longer axis, which properly belongs to the expulsion time.[1] The apex is, therefore, retracted. Such a retraction of the apex causes a retraction of the thorax, even when there are no adhesions between the pericardium and the thoracic wall; for the space left by the shortening of the heart cannot be filled quickly enough by the lung margins to prevent the thoracic walls being forced inward by the atmospheric pressure. If the adhesions between the leaves of the pericardium be not cicatricial, however, there need be no anomaly in the apex-beat. In any case, pericardial adhesions cannot be diagnosed from this phenomenon with any certainty except when an apex-beat cannot be made out to the left of the retracted region, and when this region itself includes the greater part of the precordia. This diagnosis is, of course, much assisted by the history of a preceding pericarditis.

The cases of extensive adhesions between the pericardium and the thorax have recently assumed a practical importance, since Brauer has proved that this condition, which is usually accompanied by the signs of an excessively disturbed heart action and severe cardiac disease, may be greatly helped by "cardiolysis," which consists in the removal of the bony and cartilaginous parts of the thorax wall covering the heart. By this operation the heart is spared from expending a large part of its force in the active retraction of the thoracic wall, and is, therefore, greatly relieved. This procedure is, of course, useful only when there is actual adhesion between pericardium and chest-wall, not in simple adhesions between the leaves of the pericardium, which may cause similar symptoms. For the diagnosis of the former condition Brauer[2] emphasizes: (1) The wide-spread retraction of the chest-wall (ribs and lower

[1] See Tigerstedt, Physiology of the Circulation, 1893.

[2] Münch. med. Woch., 1902, p. 1072, Meeting of the naturhistorisch med. Verein in Heidelberg; Arch. f. klin. Chir., lxxi, Part 1, Transactions of the Congress for Internal Medicine, 1904 Brauer and Kuttner, Deut. med. Woch., 1906, No. 24, reports from the societies.

part of the sternum) and sometimes of the epigastrium; (2) the diastolic venous collapse (see Fig. 114, p. 198); and (3) the phenomenon which he calls the thoracic diastolic "rebound" (Schleudern). By this term he means the strong diastolic rebound of the chest retracted during systole. On auscultation this generally gives a clapping sound lagging after the normal second tone, so producing a kind of gallop rhythm. As the systolic retraction may indicate a simple adhesion of the leaves of the pericardium without involvement of the thorax, the thoracic rebound is the most important indication for operation. It shows that the chest is forced inward during systole, not simply by the outer atmospheric pressure, but also by an active pull from within the thorax, which relaxes during diastole and causes an elastic rebound. Brauer himself, however, has noted that the thoracic rebound with gallop rhythm is sometimes observed also in certain forms of hypertrophy of the heart, particularly in chronic nephritis, a fact which he explains by his theory of the active nature of diastole. In these cases, to be sure, there is no systolic retraction, but an apex-beat. Still, as the apex is not always accessible to examination, isolated cases might occur where the diagnosis would be doubtful, so the demonstration of a previous pericarditis is in many cases a very essential indication for cardiolysis.

DOUBLE HEART-BEAT; CARDIA BIGEMINUS; HEMISYSTOLE; SYSTOLIA ALTERNANS; PSEUDOHEMISYSTOLE

Two heart-beats may, under certain conditions, follow one another very quickly, and pairs or groups of two heart-beats be separated from other pairs by a longer pause (double stroke of the heart). There results one of three distinct forms of cardiac activity, distinguished by the titles: *cardia bigeminus, hemisystole,* and *systolia alternans.*[1] According to Unverricht,[2] these three merge into one another without any sharp boundary, and are, so to speak, genetically related. Thus far they have been observed only in heart disease, especially in mitral lesions combined with tricuspid insufficiency.

With *cardia bigeminus* a peripheral arterial pulse corresponds both to the first and to the second of the double heart-beat, thus producing a sort of pulsus bigeminus (Figs. 60, 79, and 81). If there should be a venous pulse, each beat of the heart would also produce a distinct venous pulse. It is here usually a case of regularly repeated extra systoles, the arterial pulse of the extra systole being smaller than the regular pulse. (See p. 153.) It may also be due to the group formation described on p. 159.

If the second contraction of the left heart become progressively weaker until it finally disappears, perhaps from some obstacle or from a nervous influence, and if at the same time both contractions of the right heart remain distinct, *hemisystole* results. In this condition, then, the right heart beats twice for each single beat of the left heart. Such a condition was formerly diagnosed in a tricuspid insufficiency, where a double heart-beat was localized most plainly over the right ventricle, where the radial pulse corresponded only to the first beat, but where a positive venous pulse in the neck corresponded to both beats.

Systolia alternans arises from hemisystole when the first of the two beats of the right heart becomes weaker and finally disappears. According to earlier views, this peculiar condition might be determined in a ventricular venous pulse. The radial pulse unaccompanied by a venous pulse would correspond to the first beat of the heart (left), and the venous pulse unaccompanied by a radial pulse to the second beat of the heart (right). Here contraction alternates between the right and left sides of the heart.

The following scheme explains clearly the transition from one to the other:

		First heart-beat.	Second heart-beat.
Cardia bigeminus	Right heart.	Effective.	Effective.
	Left heart.	Effective.	Effective.
Hemisystole	Right heart.	Effective.	Effective.
	Left heart.	Effective.	Ineffectual.
Systolia alternans	Right heart.	Ineffectual.	Effective.
	Left heart.	Effective.	Ineffectual.

It is self-evident that valvular murmurs which could be localized would be of great assistance in distinguishing these three forms of heart-beat, which Unverricht has so cleverly pictured as modifications of one another.

[1] [For these terms the expressions, twin beat, half-beat, and altered beat of the heart may be employed.—Ed.]

[2] Berlin. klin. Woch., 1890, No. 26.

Most authors, however, agree with Riegel[1] and not with Unverricht. The former considers that the bigeminus is the only type of double heart-beat which has been conclusively demonstrated in man; and that the hemisystole, first described by v. Leyden,[2] and the systolia alternans assumed by Unverricht, in reality belong to the bigeminus.

That this is true, so far as hemisystole is concerned, is proved, according to these authors, by the fact that where an arterial pulse is not palpable for the second heart-beat, it can still be appreciated in the sphygmogram; and, according to Riegel's plausible theory, the venous pulse suffers less than the radial; because for a radial pulse it is necessary that the contraction of the left ventricle be still able to overcome the arterial blood-pressure. Here the so-called hemisystole should be regarded as a bigeminus in which the second heart-beat is so weak that it is noted only in the venous pulse and in the sphygmogram, but cannot be felt at the wrist—in other words, a "*pseudohemisystole.*" Although physiologists have for a long time demonstrated hemisystole upon the exposed mammalian heart, thus far there has been too little clinical observation to determine whether it does actually appear in man. Unverricht drew his conclusions[3] about systolia alternans, not from the alternation of the positive venous pulse with the radial pulse, but from less certain criteria, viz., the different location of heart tones, murmurs, and the beats in the two heart actions. The existence of systolia alternans must, therefore, be left undecided. (See p. 152.)

A double heart-beat may quickly alternate with normal heart activity. We do not yet know how to explain the cause of such a peculiarity, nor its prognostic significance.

INEFFECTUAL (FUTILE) HEART CONTRACTIONS

Quincke and Hochhaus[4] designated by this expression peculiar cardiac contractions which occur in heart disease, and which are characterized by the insertion of a beat between normal contractions, sometimes periodically, sometimes quite irregularly, and especially by the disproportion between the increased intensity of the heart-beat and of the first tone, on the one hand, and the weakness of the corresponding arterial pulse on the other. *Further peculiarities of these futile contractions* are: the diastolic tone is weakened and premature; the abortive contraction itself seems premature, *i. e.*, it follows an apparently shorter and precedes a longer diastole; the systolic and diastolic murmurs accompanying such ineffectual contractions are weakened or disappear; and the cardiogram may reveal changes which it is impossible to detail here. Not infrequently patients complain of these contractions as being painful or indefinitely unpleasant, or they may describe the sensation as that of a jolt or a blow.

This phenomenon without doubt generally depends upon premature or extra systoles. (See p. 153.) Only those extra systoles are "futile" (*i. e.*, give the peculiarities just mentioned, particularly the failure of the radial pulse) which are sufficiently premature to fall within the time when the ventricle is not yet properly filled. When, sometimes, as Quincke and Hochhaus expressly noted, the futile contractions are not premature (*i. e.*, are not extra systoles) they must be due to a disturbance of the contractile power. The subjective symptoms of a jolt or blow may easily be explained by a systole through which the heart does not empty itself.

CARDIOGRAPHY

The cardiograph is an apparatus which conducts the movements of the heart apex-beat, through hollow tubes, so as to represent them graphically upon a revolving drum. The resulting curves, so-called cardiograms, have already solved a series of very important questions in heart physiology.[5]

So far the method has not been so useful clinically on account of the manifold variations in the cardiograms due to differences in—(1) the exact spot examined; (2) the amount of overlapping lung; (3) the configuration of the individual thorax;

[1] Riegel and Lachmann, Deut. Arch. f. klin. Med., vol. xxviii, p. 393; Riegel, Volkmann's Vorträge, No. 227. Again, Riegel, Zur Lehre von der Herzirregularität und Incongruenz in der Thätigkeit beider Herzhälften, Wiesbaden, Bergmann, 1891.

[2] v. Leyden, Virchow's Arch., 1868, vol. xliv.

[3] *Loc. cit.*

[4] Deut. Arch. f. klin. Med., 1894, vol. liii, p. 414.

[5] Graphische Untersuchungen über die Herzbewegungen," Zeit. f. klin. Med., 1888, vol. xiii, parts 3 and 4, p. 327; Deut. med. Woch., 1888, Nos. 15 and 18; Zeit. f. klin. Med., 1889, vol. xv, parts 5 and 6, and vol. xix, 1891, parts 1 and 2.

and (4) in pathologic cases, the size of the heart chambers. The results are, therefore, often difficult to interpret correctly.

The original apparatus was also somewhat cumbersome for practical use, but this difficulty has been obviated by the use of Jaquet's simplified sphygmocardiograph and Mackenzie's polygraph. (See p. 126.) For this especial purpose Jaquet has also devised another form of recording apparatus.[1] (See Fig. 162.)

It consists of a padded lead ring (*a*), covered with leather, which may be bent so as to conform to the surface to which it is applied. It is secured in place by a belt passing around the thorax and attached to *gg*, and by a strap fastened to *h*, passing

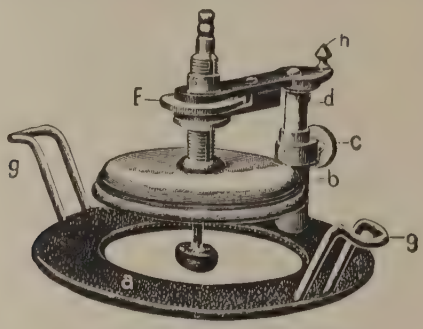


Fig. 162.—Jaquet's recording apparatus.

over the left shoulder, and attached to the belt at the back. The upright *d* can be raised or lowered by the screw *c*, and the pelotte, by the screw *f*. The pelotte should be placed as nearly as possible over the exact center of the apex-beat, and the proper pressure be attained by adjusting *c* and *f*. The simplification of the technic obtained by the modern apparatus possibly promises a more fruitful clinical use of the cardiogram in the future. Still, Mackenzie, who invented the apparatus, and who has made by far the most extensive practical use of it, points out the difficulty of a correct interpretation of the curves, owing to the great individual differences caused by variations in the point of application and the configuration of the individual thorax.

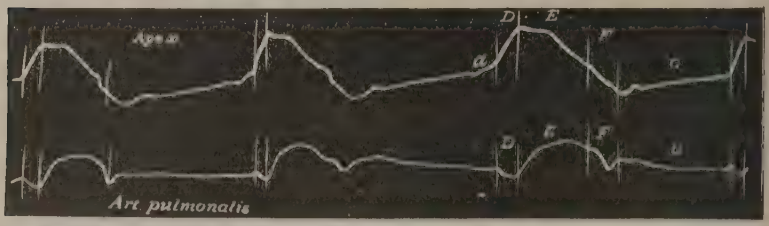


Fig. 163.—First type of cardiogram. During expulsion time the curve sinks suddenly after forming a short plateau. Simultaneous curves obtained from the apex-beat and the pulmonary artery in a consumptive with an advanced retraction of the left lung and exposure of the pulmonary artery (Mackenzie). That the second is really that of the pulmonary artery was proved by taking one of the carotid simultaneously. The letters correspond to those in Fig. 111: *D*, Closure time of systole; *E*, expulsion time; *F*, relaxation of ventricle; *G*, refilling of ventricle.

Figs. 164, 165, and 166 give some typical cardiograms illustrating some of the confusing variations. In the latter half of the upper curve in Fig. 165, we have a negative cardiogram, obtained by moving the pelotte away from the exact location of the apex-beat toward the edge of the sternum, so that the systolic raising of the apex is replaced by an apparent systolic retraction of the right ventricle. The radial curve below serves for orientation, and proves the negative character of the

[1] It may also be used in examining other pulsations, *e. g.*, the liver pulse, the pulse of the abdominal aorta, the epigastric pulsation, etc.

upper curve. Since it is often difficult to determine the exact position of the apex-beat, it is evident that a negative cardiogram might easily be obtained without its being suspected unless the radial or carotid pulse were also taken for purposes of

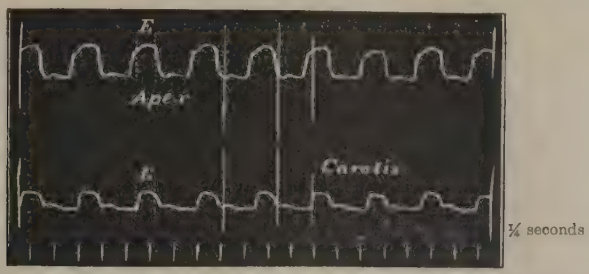


Fig. 164.—Second type of cardiogram. During expulsion time the curve rises gradually in a rounded plateau, falling off rapidly at the beginning of diastole. Synchronous curves from the apex-beat and the carotid pulse (Mackenzie). *E*, Expulsion time.

comparison. In the positive cardiograms, the apex of the radial curve should correspond very nearly to the beginning of the plateau.

The occurrence of these negative cardiograms, together with the considerations advanced on p. 361, shows that systolic retractions in the neighborhood of the apex

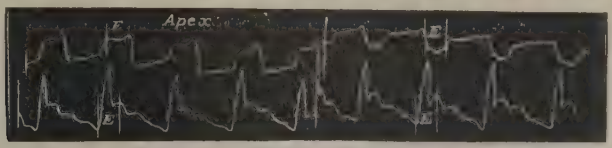


Fig. 165.—Negative cardiogram, according to Mackenzie. The first half of the upper curve shows the positive cardiogram obtained from the fourth intercostal space just outside the nipple. The second half shows the negative cardiogram obtained near the sternum in the same intercostal space. A comparison with the synchronous radial curve below shows that in the positive cardiogram the beginning of expulsion time (*E*) corresponds to a systolic rise; in the negative cardiogram, to a systolic fall.

are of diagnostic value for the recognition of pericardial adhesions only under certain fixed conditions. According to Mackenzie, a negative cardiogram may be considered in general as fixing the position of the right ventricle, as the left ventricle gives a positive curve.

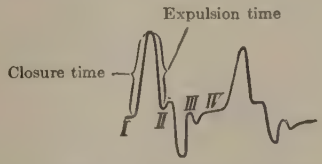


Fig. 166.—Martius' normal cardiogram: *I*, Beginning of systole; *II*, closure of semilunar valves; *III* and *IV*, recoil waves of stasis which arise in the aorta.

In regard to the interpretation of the cardiograms as given in the legends to Figs. 163 to 165, the works of Marey and Martius should be consulted. Some of Martius' cardiograms, as the one given in Fig. 166, are apparently produced by a strong rebound of the apparatus.

OTHER PULSATIONS IN THE PRECORDIA AND ITS NEIGHBORHOOD

The great vessels—aorta and pulmonary artery—are normally so thoroughly covered by the sternum and the lung that their pulsations escape appreciation. Marked dilatation of these vessels or a retraction of the normally overlapping lung makes their pulsations visible and palpable. That of the pulmonary artery appears in the second left space; that of the aorta, in the second right (Fig. 120). *Aneurysms* or the *diffuse aortic dilatation* caused by aortic insufficiency (Fig. 143) are the more common causes of the aortic pulsation, while mitral lesions are generally responsible for the pulmonic pulsation. In the latter the dilated left auricle and left ventricle push the lung aside and expose the vigorous hypertrophied right ventricle. (See Fig. 141.) If the lung be retracted by adhesions these pulsations may become evident even with a normal-sized heart and great vessels. If the heart be much enlarged, slight pulsations of the anterior ventricular wall are readily mistaken for pulsations of the great vessel trunks. In the former case the area over which the heart-beat is palpable would be larger and the pulsation felt earlier (*i. e.*, corresponding to the closure time of systole), while in the latter instance the pulsation would coincide with the expulsion time. In case of an increased area of cardiac dulness upward, the powerful heaving character of a pulsation alone should be sufficient to show that the increased dulness is due to a widening or uncovering of the arterial trunks, and not to a dilatation of the auricle. (See below.)

The systolic pulsation of an aortic aneurysm may be diffused over a considerable area, usually situated near the second right intercostal space. It is frequently visible as an expansile pulsating tumor; but is, perhaps, better appreciated by the palpating hand. If, as is ordinarily the case, an aneurysm spring from the ascending or first portion of the arch, the pulsation will generally be appreciable in the jugulum, and can be very plainly felt there as a pulsating tumor by crooking the finger behind the top of the sternum. If an aneurysm be present, the cardiogram should show the pulsation falling within the expulsion time, and, therefore, a little delayed in comparison with the apex-beat. This point is particularly serviceable for distinguishng a dilated right heart from an aneurysm of the ascending aorta, extending far down and to the right of the sternum.

The left bronchus, which is straddled by the aorta, will be depressed by each pulsation of a large aneurysm, and will, in turn, transmit this depression to the trachea, and so to the larynx. By grasping the cricoid cartilage between the thumb and forefinger of the right hand while facing the patient, the examiner can feel at the larynx this transmitted pulsation as a rhythmic systolic downward tug, the so-called **tracheal tug** (**Oliver-Cardarelli phenomenon**). [A faint tug is sometimes accentuated if the patient bend his head back and so increase the tension of the trachea. This procedure may even make the tugging visible.—Ed.] The sign should not be confused with the ordinary carotid pulsation, nor with the pulsation of the arteries of the thyroid gland, neither of which is strictly limited to a downward movement. The same sign has been plainly demonstrated in a *pulsating mediastinal sarcoma* and in *dilatation of the arch of the aorta in aortic insufficiency*, so that it can no longer be considered absolutely pathognomonic of aneurysm. The author has even observed the same sign in a man whose circulatory system was entirely normal, but in whom paralysis of the left recurrent laryngeal strongly suggested an aneurysm. The absence of other signs, however (including absence of

an x-ray shadow), the combination of paralysis of the corresponding vocal cord with that of the soft palate, and the quick recovery excluded the diagnosis of aneurysm, and the paralytic symptoms were assigned to a neuritic origin.

A short, sharp blow, corresponding to the *closure of the semilunar valves*, may be felt at the base of the heart whenever the aorta and pulmonary artery, uncovered by the lung, are exposed and situated directly behind the chest-wall. It is sometimes appreciable even without such uncovering; but never visible. Its brevity, which can be well appreciated by palpation, corresponds accurately to that of the auscultation sound of the second tone. It is to be felt most distinctly over the pulmonary artery in mitral lesions which are associated with an accentuated pulmonic second sound.

A *diffuse, feeble, systolic auricular vibration*, distinct from other cardiac pulsations, may sometimes be felt or seen at the base of the heart. It comes out especially plainly when a marked auricular dilatation from mitral or tricuspid insufficiency has pushed the lung aside. We feel, then, not auricular contraction, but auricular diastole, which in the valvular lesions mentioned above is intensified by the stasis or regurgitation at the mitral valve. In a gallop rhythm (see p. 325), the presystolic contraction of the auricle can sometimes be felt, provided the latter is not overlapped by too much of the lung.

A *systolic auriculoventricular valve shock*, the palpatory equivalent of the systolic valvular tone, and correspondingly brief, should not be confused with this auricular vibration. The former is felt in the region of the auriculoventricular valves to the right and left of the sternum, especially when marked cardiac dilatation pushes the lung aside. The ear against the stethoscope readily appreciates the difference between it and the actual heart-beat; it is not really heaving nor visible, and is much shorter and sharper than the latter.

An *epigastric pulsation*, a visible, palpable, pulsating shaking or lifting of the epigastrium, appears in emphysema. The diaphragm is low, the heart lies nearer to the epigastrium, the right ventricle is hypertrophied and may be dilated; hence the heart-beat is transmitted directly through the diaphragm to the epigastrium. A normal heart, if excited, sometimes causes an epigastric pulsation. Mackenzie has shown that the epigastric pulsation, in case it depends upon a low-placed hypertrophied right ventricle, is recorded by the cardiograph (see p. 365) as a systolic retraction, giving a negative cardiogram (see p. 365), while if it depend upon the left ventricle, the cardiogram is positive.

A pulsation of the abdominal aorta in a thin patient with retracted abdominal walls and partially filled intestines often resembles an epigastric pulsation, but a careful palpation of the abdominal aorta from below upward will generally distinguish them. This pulsation appears in the cardiogram to be almost synchronous with the radial pulse, and somewhat delayed in comparison with the apex-beat, which falls within the closure time. The same is true of the pulsation of aneurisms of the abdominal aorta.

Although we discussed *pulsation of the liver* in the section upon the Venous Pulse (see p. 192 et seq.), it should also be noted that an arterial pulse is sometimes felt over the liver. (See p. 198.) This occurs most frequently in aortic regurgitation as a result of the pulsus celer, and also in inflammatory conditions of the liver. The author has observed such

an arterial liver pulse in a case of infectious cholangitis. Mackenzie has shown that the edge of the liver may be involved in the epigastric pulsation (see above), and that it then, as the synchronous record of the radial pulse shows, moves upward during systole (negative cardiogram).

In aortic regurgitation, as a result of the pulsus celer, the spleen also may pulsate. The *splenic pulse* is presumably always arterial, because the splenic vein empties into the portal vein, which never pulsates, as it is cut off from the heart by the intervening liver.

The reader is also referred to what has been said about pulmonary pulsation and pulsating pleurisy (p. 353 et seq.).

PALPATION OF CARDIAC MURMURS

(Thrill; Fremissement)

Some heart murmurs are as plainly palpable as the heart tones. They are most readily appreciated by a light touch of the palmar surface of the hand [of its ulnar edge or of the finger.—Ed.].

Pericardial rubs are naturally very distinctly palpable. (See p. 344 et seq.)

Neither accidental nor valvular endocardial murmurs can usually be appreciated by palpation unless they are very loud and vigorous. In *mitral stenosis*, however, a distinct presystolic thrill ("purring thrill") is frequently felt at the apex, even when no murmur can be heard. This peculiarity is explained by the difference in the number of vibrations appreciated by the sense of hearing and that of touch. (See Auscultation with Reference to the Localization of Murmurs, etc., p. 337.)

INSPECTION AND PALPATION OF THE ABDOMEN

(See the section upon the Examination of the Stomach and the Intestines, pp. 422 and 500.)

Inspection and palpation, discussed here together, are more reliable in the examination of the abdomen than percussion.

INSPECTION OF THE ABDOMEN

This should be attempted first with the patient in the dorsal decubitus; afterward, if necessary, in the erect, and then in other positions. We should first notice any increase or decrease of the volume of the abdomen as a whole, the significance of which must be controlled by percussion and palpation.

Obesity is one of the most frequent causes of abdominal enlargement, for the subcutaneous tissue of the abdomen is a favorite place for the deposition of fat. The abdomen is then uniformly arched, when lying or standing; or the bulging may be somewhat lobulated, owing to

the arrangement of fat; the navel is depressed, because the connective tissue thereabout is so rigid that fat cannot be deposited. An attempt to grasp the panniculus adiposus between the fingers will solve any doubt. Percussion elicits a dulness, the intensity of which depends upon the thickness of the fat-layer. (See Fig. 2, p. 24.)

Edema of the abdominal wall presents the same retracted navel and may possibly be confused with a fat belly; but the almost constant existence of the edema elsewhere, its preponderance in the lateral and inferior portions as contrasted with the median deposition of fat, the pitting of the skin, and other clinical relations (p. 50) will solve any doubt.

Meteorism (tympanites) causes abdominal distention. It lessens or obliterates the umbilical depression unless the wall is thickened by edema or fat. The contour of the stomach or of the intestinal coils can frequently be seen through thin abdominal walls, especially when peristalsis is active or when the organs are dilated, particularly if the dilatation be dependent upon a stenotic obstruction in the digestive tract (*pyloric stenosis, ileus, intestinal tumors*). The intestinal movements in ileus are at first visibly increased; but later the distended coils, particularly those in the neighborhood of the obstruction, become paralyzed and immobile and occupy most of the abdominal surface. By noting through the abdominal wall the contour of an especially distended and completely immobile coil of intestine, the position of the obstruction can sometimes be determined. In very marked meteorism the difference in caliber between the large and the small intestine cannot be appreciated. The paralytic immobility of the visible intestinal contour and the absence of intestinal murmurs to auscultation are important signs for the diagnosis of *acute diffuse peritonitis.*

Free **accumulation of air in the peritoneal cavity** from perforation of the stomach or intestine is characterized by a uniform distention of the abdomen without visible stomach or intestinal contour.

A **collection of free fluid** also produces an apparently uniform distention of the abdomen. In the dorsal decubitus the fluid, when under no great tension, is mostly accumulated in the lateral portions, so that the abdomen seems proportionately broad. In case the fluid reaches so high, the navel (as contrasted with its position in meteorism) protrudes slightly. Percussion of an abdomen containing free fluid elicits a dulness of the dependent portions. (See p. 278.) This dulness shifts with change of position. Still more essential to the diagnosis of free fluid is the so-called *fluctuation wave* (see p. 373), which can sometimes, when the patient is moved, be appreciated, even by inspection, as a characteristic flopping. If the tension of the abdominal contents be increased, this flopping is not visible, but frequently the peculiar way in which a patient's movement makes the abdomen fall to one side like a heavy body shows the presence of fluid, in contrast to mere meteorism.

The presence of **distended veins in the abdominal wall** (p. 60 et seq.) aids in diagnosing the cause of the free fluid in the abdominal cavity. If they be limited to the sides of the abdominal wall (Fig. 20), and if an examination show that they conduct the blood from below upward, they present the type of collateral circulation observed most plainly in *thrombosis* of the *vena cava inferior.* In this case a part of the blood which should proceed through the vena cava inferior is deflected, and flows directly from the lower extremities,

through the veins of the anterior abdominal wall, into the vena cava superior. Any fluid effusion in the abdominal cavity might compress the vena cava inferior enough to cause some obstruction; hence, this sign of a collateral circulation is of slight value unless the venous distention be very marked. Then it would point to an actual thrombosis of the inferior vena cava. On the contrary (p. 61 et seq.), distended veins which occupy more the middle of the abdominal wall, radiating from the umbilicus in the form of a so-called "caput Medusæ," and whose blood-current plainly flows in every direction from the umbilicus, would point to an anatomic *obstruction of the portal circulation* (*cirrhosis of the liver, thrombosis of the portal vein*). It must be acknowledged that this radiating arrangement is not a striking factor in every case of portal obstruction, but its median position and the direction of the blood-current away from the navel is constant enough to be of diagnostic value. (See Fig. 21.) One might think that the high pressure of any effusion in the peritoneal cavity would cause a certain degree of portal stasis from its compressing action, and therefore produce a similar collateral circulation. Yet experience shows that this type of collateral circulation is practically limited to *cirrhosis of the liver* and to *portal thrombosis*. This becomes perfectly explicable when we realize that the small anastomotic branches, lying between the portal vein and the area of the vena cava, which are essential to the formation of this collateral circulation, are just as much compressed by a peritoneal effusion as is the portal vein itself. (See p. 60 et seq.) It is a different thing with the portal stasis in a limited sense, which arises from a portal obstruction due to hepatic cirrhosis, or due to thrombosis of the portal trunk near its entrance to the liver. The collateral circulation is then undertaken by the veins of the ligamentum teres and of the serous covering of the liver, for they connect with the portal system at a point above the obstruction (upstream).

Large ovarian tumors or *other abdominal cysts* are differentiated from effusions of free fluid by inspection, palpation, and percussion (p. 278 et seq.). With them the greatest degree of prominence and resistance is in the median line of the abdomen, not in the more dependent portions. But all other methods of examination must frequently be employed for a certain differentiation.

Enteroptosis presents to inspection a peculiarly characteristic and practical clinical picture. This condition depends upon a relaxation of the abdominal walls and of the mesentery. It is more frequently observed in the female sex, and is due either to a marked loss of the subperitoneal, submesenteric, and subcutaneous fat, and to an atrophy of the abdominal muscles, or, following pregnancy, to an impaired tension of the stretched abdominal walls and peritoneum. In the latter case there is almost always associated a loss of fat of the abdominal walls and of the abdominal contents, a certain degree of atrophy, and frequently even a spreading of the recti muscles. As a consequence the abdominal organs are abnormally mobile; the liver and the kidneys in the erect posture are situated lower than normal; the right kidney especially gradually draws down a mesentery for itself and becomes a movable, or even a genuine floating, kidney. Without sufficient support the stomach and transverse colon may drop and sink deep into the abdomen. The weight of its contents causing passive distention, frequently dilates the stomach. When the physiologic support of the

abdominal wall fails, the intestines become distended with gas. The skin of the abdomen becomes lean, withered, and frequently wrinkled; in patients who have borne children it is covered with striæ. The walls are so thin that the contour of the stomach and intestines, especially in the dorsal decubitus, can be made out very plainly. In the erect posture a veritable paunch is noticed, and through the gaping breach between the recti muscles a considerable portion of the abdominal contents projects like a hernia.

Empty intestines in **inanition,** *e. g.*, from starvation or esophageal stenosis, produce a very decided retraction of the abdomen. A similar appearance in tuberculous meningitis—the so-called "scaphoid belly"—is due to a contraction of the intestinal muscles, and perhaps of the abdominal muscles as well. Inspection sometimes reveals local prominences (cysts, tumors, enlargement of the abdominal organs) and their mobility with respiration.

PALPATION OF THE ABDOMEN

METHOD OF PALPATION

The first requisite is a thorough relaxation of the abdominal walls. Therefore, if his condition permit, place the patient in the dorsal decubitus, take away everything from under his head except a very thin pillow, and get him to breathe quietly, regularly, and without exerting abdominal pressure. Sometimes flexing the knees slightly will help to relax the abdominal walls. For palpating the lower portion of the abdomen it is frequently advantageous to raise the buttocks by putting a number of pillows under them, or to place the patient on an examining table in the Trendelenburg position. This frequently relaxes the abdominal walls to a marked degree, and pushes the abdominal organs toward the diaphragm, thus allowing the lower part of the abdomen to be more easily palpated. Considerable tension of the belly, if due to meteorism, can frequently be relieved and the examination be facilitated by first emptying the colon of feces and gas with the aid of a copious water enema. Great tension and extreme sensitiveness of the abdomen may necessitate the employment of anesthesia. It should, therefore, never be neglected in any serious and doubtful case if there be a question of an operation, as the absolutely relaxed walls under anesthesia enable the examiner to make a more thorough examination [1]

The physician himself can prevent a reflex spasm of the abdominal muscles by his method of palpation. If his hands be cold, they should be warmed before he touches the patient's belly. He should not palpate with the finger-tips, but always with the flat of the hand, with gradually increasing pressure. All hurried movements annoy the patient, render the examination difficult, and are therefore to be avoided. The more superficial should precede deeper palpation, because the former is less disagreeable to the patient. The expiratory retraction of the abdominal walls enables one to press the hand gradually deeper. At first the hand should be placed upon the spot to be examined, and

[1] According to the author's view, an examination under anesthesia should be limited to the determination of some condition which might require a decided change in therapy. He emphasizes this because such examinations and exploratory laparotomies, the former sometimes not less dangerous than the latter to the patient's well-being, are often abused.

left there quietly during both inspiration and expiration. The way the parts under the hand move during the respiratory excursion should be noted; and only after this procedure should tactile movements be made use of to feel the entire abdominal surface. In palpating painful affections it is a good rule to begin with the painless parts, thus gaining the patient's confidence and distracting his attention. This is especially to be recommended in examining children. The examiner's hand should rest as comfortably as possible, otherwise its sensitiveness is impaired. Bimanual palpation frequently furnishes very useful results; one hand placed upon the lateral or anterior surface of the abdomen presses the parts against the other hand in the flanks, in the vagina, or in the rectum.

In all difficult cases it is of decided advantage to palpate in different positions of the body, *e. g.*, in the dorsal decubitus, the right and left lateral, the erect, the knee-chest posture, the elevated pubic posture, and the Trendelenburg posture.

Rubbing the skin of the abdomen with oil or, even better, with powdered chalk frequently facilitates an examination. The palpating fingers slip over the skin more readily, and so their sensitiveness is increased. This device makes palpation less disagreeable and less painful to the patient, and is, therefore, to be recommended. [A simple and frequently helpful expedient for relaxing the abdominal muscles during palpation is immersing the patient in a hot bath.—Ed.]

Jerky or interrupted palpation [" *dipping.*"—Ed.] is often advantageous for certain purposes. The palpating hand is placed flat upon the part of the abdomen to be examined; then quite powerful but short strokes are employed with the flat of the hand or sometimes with the fingers. This method may demonstrate the *collection of fluid* in the abdomen, or the presence of *deeply placed solid masses* covered by fluid which ordinary palpation does not reach. In favorable cases the deeply placed solid parts, if movable, seem to strike the palpating hand, because the blow excites a great wave movement in the fluid. The same method of palpation is employed in obstetric examinations—the so-called "ballottement" of the fetal head. "Dipping" can be recommended to demonstrate *enlargement of the liver or of the spleen, deep-lying tumors or a distended gall-bladder,* and for palpating an abdomen tensely distended with fluid where ordinary palpation as well as percussion leaves one in doubt.

An important rule in palpating the abdomen is to proceed very cautiously, since roughness can very easily do harm, especially in acute inflammatory affections.

GENERAL RESULTS OF ABDOMINAL PALPATION

Abdominal palpation should appreciate the general condition of resistance in the belly (both of the walls and of the abdominal contents), the palpable boundaries of the organs, their sensitiveness to pressure, and any local resistance and tumors. Palpation then quickly confirms, completes, and corrects the results of inspection in regard to the presence of fat-accumulation, of edema in the abdominal wall, of fluid within the abdominal cavity, or of meteorism. Interrupted palpation [eliciting the "fluctuation wave."—Ed.] is the best method of demonstrating fluid. One hand strikes a short, sharp blow upon one side, over a dependent portion where the fluid is suspected, and if fluid be really

present, the other hand, upon a diametrically opposite spot of the abdomen, will then feel a plain wave shock. *Fluctuation*, in the ordinary sense of the word (*i. e.*, the transmission of slow pressure movements through the abdomen), cannot be relied upon to demonstrate fluid in the belly, because the normal intestines filled with air fluctuate in that sense. The distinct transmission of short blows is, on the contrary, quite characteristic of the presence of fluid rather than of gas, because the phenomenon requires a considerable mass and there is the delay of inertia in the moved substance.

Enteroptosis presents to palpation an abnormal thinness and flabbiness of the abdominal walls and hyperesthesia. The organs may all be palpated and bounded just as if there were no covering. Tense intestinal coils and a stomach distended with gas are often much more readily outlined by palpation than by percussion, on account of their firm resistance, like that of an air-cushion. Contracted intestinal loops feel like tubes, varying in size from the little finger to the thumb. They are generally movable enough to be rolled under the finger. The "haustra" of the large intestines can sometimes be plainly felt. In palpating abdominal organs their respiratory mobility is always important. (See Special Palpatory Relations of Certain Abdominal Affections.)

In palpating *tumors* or *pathologic resistances* we should carefully heed their position, their form, their size, the possibility of outlining their boundaries, their consistence (solid, hard, compact, elastic, fluctuating [1]), the character of their surface (smooth, nodular), and their sensitiveness to pressure. We should then determine from what organ the tumor arises; whether it is covered by the stomach or by the intestines, etc. Artificial distention of the stomach or colon will often clear up this part of the examination. The stomach can be distended either by means of an effervescing powder or by inflation through a stomach-tube. (See Gastric Examination.) The colon is most conveniently inflated by means of [an ordinary Davidson syringe.—Ed.].[2] Inflation will conceal from inspection, percussion, and palpation tumors which are situated behind the stomach or colon or in their posterior walls.

In determining *tenderness* very gentle palpation is first employed. If this produce no pain, more force is used. We should then determine whether there is sensitiveness to quiet and regular pressure or only to displacement of parts, for in many cases the tenderness is produced only by a blow, not by mere pressure. This is frequently the case in peritonitis. After we have demonstrated the existence of tenderness, we should always attempt to differentiate at what depth it is situated. By pinching up the skin or the entire abdominal wall in a fold we can readily prove whether it is merely a sensitiveness of the abdominal wall and of the skin or whether it arises from the abdominal contents. If we can determine a hyperalgesia of the unaltered skin, even to light touch or to pinprick, over the painful area in any doubtful painful affection of the abdominal contents, the pain in question is not alone peripheral (organic pain), but is either

[1] There is a special sort of fluctuation, the so-called "hydatid thrill," which is sometimes appreciated over echinococcus cysts by striking a blow upon one spot of the tumor. The thrill proceeds from the impact of the daughter cysts.

[2] It is frequently necessary beforehand to cleanse and empty the rectum thoroughly with a copious enema of water.

increased or exclusively caused by central stimulation; in other words, the patient's suffering depends upon more than an anatomic change limited to the abdominal contents. (See Examination of the Nervous System; Hyperalgesic Zones of the Skin in Diseases of Deep-lying Organs, p. 983.) Cutaneous hyperalgesia plays an important rôle in the diagnosis of pseudoperityphlitis. This is a painful condition of the ileocecal region, which often arises psychically, especially since public attention has been more and more attracted to the vermiform appendix. Such psychic ileocecal pain is frequently responsible for an unnecessary operation. The sensitiveness to pressure in gastric ulcer belongs, for the most part, to these hyperalgesic irradiations. It does not, as was formerly supposed, correspond to the position of the ulcer, since the usual position is but slightly accessible to direct pressure; but the epigastric pressure point directly under the xiphoid cartilage, and the pressure points to the left of spinous processes of the dorsal vertebræ are to be regarded as neuralgic pressure points in consequence of the radiating increased irritability in the area of the corresponding segments of the spinal cord.

SOURCES OF ERROR IN PALPATING THE ABDOMEN

The abdominal walls frequently resist palpation with a vigorous reflex tension which no device can control, even under perfectly physiologic conditions. The individual parts of the abdominal wall, especially the muscular bellies and tendinous bands of the recti, vary considerably both in their tension and in their resistance, so that they sometimes produce the impression of circumscribed tumors, or, at least, of pathologic resistances. This is even more striking when the section of the abdominal muscles lying directly over the affected parts becomes reflexly contracted and more tense (muscle on guard). Abdominal pressure will facilitate the recognition of such tense muscle bellies, *e. g.*, coughing will make their contour still plainer. Examination during coughing or during increased abdominal pressure is an especially useful means of differentiating whether tumors or resistances are situated beneath or within the abdominal wall. Tension of the abdominal muscles from coughing will cause the resistance to disappear if beneath the abdominal wall. If situated in the wall itself, a tumor or resistance either becomes more distinct, or, at least, remains just as plain during coughing. The lobules of fat of the panniculus adiposus may simulate a nodular growth within the abdomen. The same methods may be used to prevent this source of error. Contracted intestinal coils are often plainly felt through thin abdominal walls, as if they were cords. (See p. 373.) The cylindric contracted transverse colon running across the abdomen is often mistaken for a tumor of the stomach or for a tuberculous degenerated and contracted omentum. The characteristic mobility of the transverse colon, which we can ordinarily roll under the palpating finger, the palpable recognition of the haustra, and finally the results gained by the distention of the colon from the rectum (p. 373), will generally prevent a mistake.

Fecal tumors frequently cause an error in diagnosis. These are collections of feces in the colon, sometimes in the form of large, compact masses, sometimes in that of smaller tumors arranged in a row, like a string of beads. Constipation usually accompanies such phenom-

ena; but fecal tumors are sometimes observed even in patients whose bowels move daily. They present a peculiar, somewhat doughy consistence: they can frequently be crumbled into smaller pieces; they are often arranged characteristically, like a string of beads; and their position in the course of the colon and the sigmoid flexure is suggestive. The coincidence of constipation, the lack of serious symptoms, and the disappearance of the masses after purgatives or enemata should prevent an error in diagnosis. Epigastric or aortic pulsations may sometimes simulate a tumor [or an aneurysm.—Ed.] (p. 367). If such a pulsation be transmitted to a tumor, the latter might be taken for a pulsating tumor. Remembering this should be sufficient to prevent the mistake.

SPECIAL RESULTS OF PALPATION IN CERTAIN AFFECTIONS OF THE ABDOMEN AND ITS ORGANS

Inflammatory exudates are appreciated by the examiner as imperfectly or perfectly circumscribed tumor-like resistances. They are almost always passive and immovable with respiration. *Perityphlitic exudations* are inflammatory exudations characterized by their peculiar location about the cecum. In spite of the presence of pus (*e. g.*, appendicular perforation and abscess) they may exhibit a very firm consistence, but this distinction no longer has any practical value, since the so-called "stercoral" tumors are now known to be inflammatory exudates and phlegmonous infiltration, quite frequently even collections of pus. It is now believed that all inflammatory conditions of the cecal region are of the same character, are infectious and usually start in the appendix or cecum, and that their differences are only those of degree.[1] A firm tumor (as contrasted with a diffuse resistance) is very likely due to the formation of thick adhesions and localized infiltration and exudation. Such forms are also frequently perforative, despite their generally favorable outcome. The long-continued persistence of such a tumor, despite the lack of all serious phenomena, is one of the most trustworthy signs of an abscess which for the time being remains quiescent. Wherever, despite the most serious symptoms, the

[1] See the author's paper upon "The Pathology and Treatment of Typhlitis," der Behandlungen des XIII. Cong. f. inn. Med. in München, 1895, Bergmann, Wiesbaden.

Although in this article the author helped to discredit the then fully current conception of a stercoral typhlitis, and to urge operation for certain forms of perityphlitis, he by no means intended to assist the tendency toward neglecting diagnosis in cases of ileocecal pain. So far has this tendency now carried the profession that every pain in that region is looked upon indiscriminately as a sign of appendicitis. And yet it is certainly true that simple constipation, wind colic, diffuse enteritis—all can cause pain located in the ileocecal region. Intestinal pain is due to increased pressure of the intestinal contents. (See Nothnagel, Zur Pathogenese der Kolik, Arch. f. Verdauungs-Krankheiten, vol. xi, and Meltzer, Bemerkungen über Gastralgia, Magenkolik und Kolik in allgemeinen, New York German Med. Soc., April 6, 1903; reprinted in Arch. f. Verdauungs-Krankheiten.) The presence of the ileocecal valve prevents this increased pressure from being equalized in the cecum, in contrast to other sections of the intestine, as the intestinal contents can move only in one direction, and even in that direction their progress is frequently prevented by impacted feces. Hence, intestinal pain is apt to center in the ileocecal region. The present generation of practitioners have in general been taught to judge the question of appendicitis from a one-sided point of view, ignoring physiology in favor of surgery. Hence these important facts of pathologic physiology, and the frequent picture of ileocecal pain with no involvement of the appendix have completely vanished from the mind of the majority of practitioners. This explains the present blind zeal for operation, inconceivable to the scientific minded physician, and disgracing the name of medical science. Year after year countless appendices are removed when no appendicitis nor, in general, any abnormal condition of the appendix is found. We are in the midst of a raging epidemic on the part of both the laity and the profession, which coming decades will deride with the same justice with which we in our day condemn the bloody vampire of the Broussais school with their routine blood-letting.

resistance remains merely diffuse, a grave state of affairs ordinarily exists, and, frequently enough, primary diffuse perforative peritonitis. Roux considers as an especially characteristic sign of pus formation the doughy, edematous infiltration of the cecal wall, appreciable to palpation (like moist pasteboard). Even large perityphlitic abscesses do not furnish any fluctuation until very late in their course. The abdomen itself, on account of its air contents, frequently fluctuates to a certain extent. A perityphlitic abscess lies deeply and is surrounded by yielding walls; hence fluctuation is absent or indistinct. If the walls should be firm, the resistance from the infiltration would prevent the appreciation of fluctuation. Not infrequently we can palpate a sort of swashing, gurgling, or splashing over a perforated perityphlitic abscess, because it contains gas and fluid. But intestinal coils which contain air and fluid furnish the same sign, so that it is not diagnostic of a gas-containing abscess unless it be permanent and very striking over an area where the presence of a large, firm, and superficial tumor makes the presence of a normal intestinal coil improbable. A cylindric, rope-like body, corresponding in its form and its position to an enlarged appendix (*i. e.*, inside and below the cecum, at the edge of the true pelvis), will, especially if it be sensitive to pressure, support the diagnosis of a previous attack of appendicitis, and sometimes will furnish a strong argument for an interval operation. A contracted intestinal coil might cause confusion. One must beware of autosuggestion.

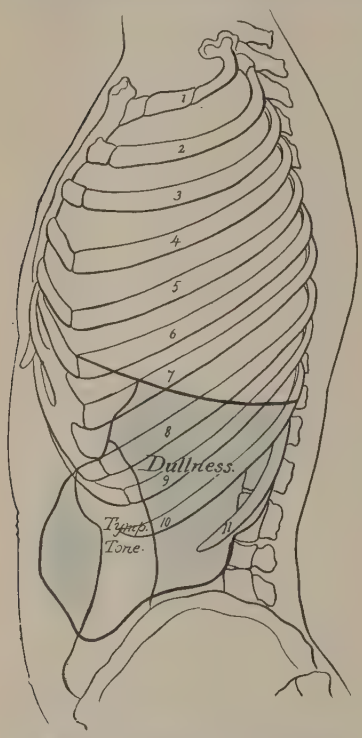


Fig. 167.—Sarcoma of the kidney, with the descending colon pushed to one side and forward.

A tumor, in the anatomicopathologic sense of the word, is appreciated as a firm, often hard, and lumpy mass. Tumors of the intestine (those of the colon are much the commonest) are best distinguished by the resulting intestinal stenosis and by their mobility, which latter, unless adhesions occur, is much more marked than with any other abdominal organ. Tumors of the stomach are generally recognized with ease, both by their position and by the accompanying gastric symptoms. They are most frequently situated at the pylorus. Despite a very wide-spread opinion, they should not be searched for much to the right of the median line, because, as a result of the curved form of the stomach, the pylorus reaches only slightly to the right. (See Fig. 120.) Moreover, gastric tumors frequently lead to dilatation, and therefore to alterations of the position of the stomach. Hence they may be found very low in the abdomen and quite extraordinarily even in the pelvis. The best way to determine the relations of a *gastric tumor* is to examine the stomach both when it is empty and when it is distended with gas. (See Examination of the Stomach, p. 422.) Gastric tumors are generally but slightly movable with respiration; but there are countless exceptions.

Renal tumors, which appear in the loins, can scarcely be pushed forward by the posterior palpating hand. Besides, while growing forward, they still remain covered by the hepatic or splenic flexures of the colon. This covering can be plainly demonstrated to percussion, palpation, and inspection (Fig. 167), by inflating the colon with gas, [inserting an ordinary Davidson syringe in the rectum.—Ed.]. If we inflate by jerks, inspection and palpation will probably show the anterior position of the colon most distinctly. Renal tumors sometimes, but not necessarily, move with respiration. *Hydronephrosis* gives rise to a renal tumor which is char-

acterized by an elastic consistence, and sometimes also by a change in size coinciding with the alterations in the amount of urine.

Tumors of the liver and of the *spleen* are characterized by their position and by their relation to organ boundaries, which we can definitely palpate and percuss, and also by their marked mobility with respiration.

Tumors of the *mesenteric* and *retroperitoneal glands* are characterized chiefly by their multiplicity; by the rounded contour of the individual tumors; by their deep position underneath the intestines, recognized by percussion as well as by palpation; and by their etiology, for they are generally metastatic. *Tuberculous retroperitoneal and mesenteric glands* present similar conditions. *Tuberculous tumors of the peritoneum* are palpated as nodular or irregularly defined resistances. The *tuberculous infiltrated* and *retracted omentum* presents a very characteristic picture. It can be felt as a knobbed cord between the xiphoid cartilage and the navel running horizontally and superficially. It may sometimes closely simulate an enlarged and uneven liver ("tuberculous pseudoliver"). *Tumors of the bladder* and *tumors growing out from the pelvis* are characterized by their position, which can be more accurately established by means of a rectal or vaginal examination.

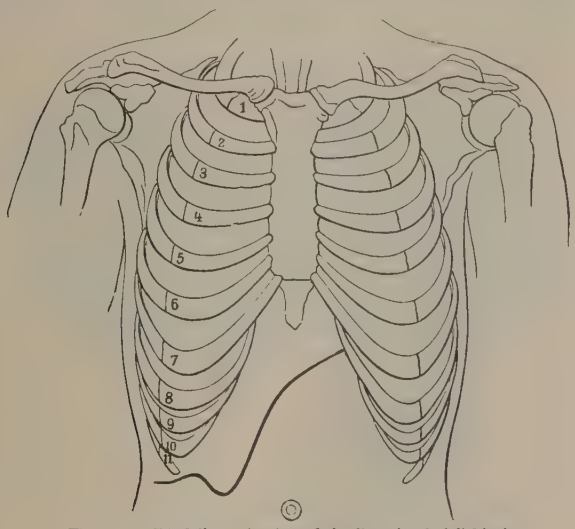


Fig. 168.—Riedel's projection of the liver in cholelithiasis.

Diffuse enlargements or *low position of the liver* are recognized quite easily by the shape of the resistance; the determination of the sharp edge of the liver; and the respiratory mobility. The diminution in the size of the liver in *acute yellow atrophy* and in *cirrhosis* can safely be diagnosed by palpation and percussion only where the previous position of the liver edge has been known. The normal liver is, however, not always palpable, depending upon the thickness of the abdominal covering and upon the extent of the respiratory excursions. In palpating the liver border it is often very important to recognize the normal notch at the insertion of the ligamentum teres. *Enlargement of the gall-bladder* from biliary stasis, gall-stones, or empyema may be characteristically localized by palpating just to the right of this notch, where we can frequently very plainly follow the sharp edge of the liver above the rounded or gourd-shaped tumor, the gall-bladder. Occasionally we can feel one very large or countless small gall-stones inclosed in the enlarged gall-bladder of a gall-stone affection. Any hard places are usually caused by an inflammatory thickening of the wall or by carcinomatous infiltration, which so frequently follows old cases of cholelithiasis. "*Dipping*" (*i. e.*, jerky palpation) over the enlarged gall-bladder will sometimes bring out a crepitation or grating of the gall-stones upon one another. If we cannot feel the enlarged gall-bladder in cholelithiasis, we frequently can feel a peculiar, tongue-like projection of the

liver drawn out by the enlargement of the gall-bladder and situated directly above it (Riedel) (Fig. 168). A similar or even larger projection can be determined over the corset liver (Fig. 169). Alterations in the liver consistence, *e. g.*, the characteristic induration of cirrhosis, can be easily recognized at the thin, sharp liver edge, provided the patient has thin and relaxed abdominal walls. The large lumps or nodules of the lobulated syphilitic or carcinomatous liver are still easier to feel.

It is generally easy to palpate a *dislocated* or *movable kidney*, especially if the dislocation be marked (*true floating kidney*). It is commoner upon the right side. It is best, in difficult cases, to relax the abdominal walls as much as possible and to push with left hand in the lumbar region forward against the right hand, which palpates the organ from in front. A movable kidney can then be recognized as a bean-shaped, vertically placed body between the two palpating hands. At times it is somewhat sensitive to pressure. At the height of inspiration it may be partially grasped between the two hands. The deep location (generally beneath the resonant colon), the verification of the upper bluntly rounded end of the kidney, the lack of any sharp edge which could correspond to the liver border, should prevent confusion with a corset liver. Sometimes the hilum and the pulsating renal artery on the concave side of the kidney can be felt. With this condition the abdominal walls are frequently much relaxed, so that it is sometimes possible to feel a dislocated kidney better in the standing or sitting, than in the recumbent, posture. If the walls be

Fig. 169.—Corset liver (Frerichs).

very relaxed, the lower end of even a normally placed kidney may be felt. A disregard of this fact has led to the diagnosis of entirely too many "wandering kidneys."

Diffuse enlargement of the spleen, acute splenic swelling, passive congestion of the spleen, the spleen of leukemia, of *pseudoleukemia*, and of *intermittent fever* are all very easily palpated and determined by their position, shape, and mobility with respiration. The very large splenic tumor of leukemia and malaria often shows one or more horizontal notches on the anterior edge (Fig. 170), and its anterior surface is generally smooth (occasionally rough in leukemia) and reaches some distance below the navel. Acute splenic swelling in *typhoid fever* and *other infectious diseases* can sometimes be demonstrated only at the height of inspiration when the inferior edge is felt just below the costal margin. This is of far greater diagnostic import than the results of splenic percussion, which, as we have seen, are frequently untrustworthy, especially if but one examination be made. In adults a spleen of normal size can only very exceptionally be palpated beneath the rib margin, even with deep inspiration, and then the abdominal walls are generally very lax or the organs are dislocated (floating spleen, enteroptosis). In young children, however, this is frequently possible, and therefore with them one must be rather cautious in diagnosing splenic enlargement. To recognize a moderate grade of splenic enlargement by palpation we should examine both in the dorsal decubitus and in the right semilateral position (diagonal position). Sometimes one and sometimes the other

position furnishes better results. In palpating the spleen, stand, if possible, upon the right side of the patient, place the palpating right hand as flat as possible upon the left hypochondrium, with the fingers at the costal margin, and with each expiration gradually exert slightly more pressure and attempt to feel the edge of the spleen during deep inspiration. Especially in typhoid fever a splenic enlargement can be felt only at the end of deep inspiration. In very sick cases the best method is from time to time to encourage one or two deep inspirations, because frequently repeated respiratory efforts tire the patient and his breathing becomes very superficial. Trying to feel the spleen with the fingers hooked in under the rib margin from above ordinarily produces such vigorous reflex abdominal contraction that nothing can be felt. Correct splenic palpation requires much practice. It is a good preparation for abdominal palpation. [Most beginners are apt to employ too great force in palpating for the splenic edge.—Ed.]

Large left-sided pleural effusions sometimes, though exceptionally, dislocate the spleen sufficiently for it to be palpable. Ferber explains this peculiarity (his opinion is supported by postmortem researches) in this way: Such effusions push the spleen so that the posterosuperior end reaches forward, the inferior end, back-

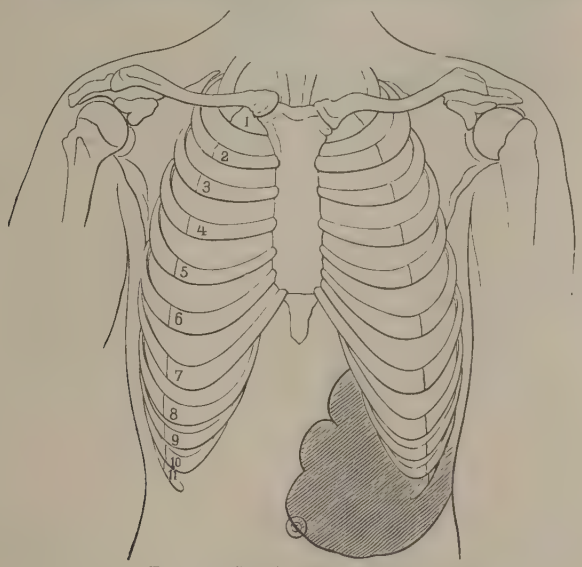


Fig. 170.—Splenic tumor of leukemia.

ward; hence the long axis of the spleen assumes at first a vertical position, and finally a direction from in front and above backward and downward. In other cases the upper edge of the spleen is turned so toward the interior by the inferior convexity of the diaphragm that the splenic surface lies no longer vertically, but horizontally. Both results are thoroughly unfavorable for palpation, and, besides, the respiratory mobility is lost, because the diaphragm on that side is almost stationary. What we often mistake for the spleen in these cases is the bulging of the depressed diaphragm running parallel to the costal border. (See Fig. 147, *I*, p. 268.)

(Compare the section on Examination of the Stomach in regard to the palpability of the spleen in certain cases of gastric dilatation.)

A *distended bladder* (see Fig. 171 upon next page) is easy enough to recognize after it has once been felt. It may be confused with the pregnant uterus, with other enlargements of the uterus, with ovarian tumors, and with inflammatory exudates. To differentiate, we must utilize other methods of examination, *e. g.*, by vagina, and especially examination after catheterization.

A *peritoneal friction* may be appreciable to palpation over the different organs or over tumors of the abdomen. The friction can be felt as a rough grating with

the respiratory and palpatory moving of the parts. It may also be appreciated by auscultation. (See p. 352.) These friction murmurs can be produced by any uneven surface (tumor surface), but in most of the cases they are caused by inflammatory deposition of fibrin. Splenic enlargement (in leukemia) frequently leads to perisplenic, and cholelithiasis to perihepatic, friction murmurs.

Peristaltic intestinal noises can also be appreciated by palpation. (See Section on Auscultation of the Abdomen, p. 352.)

"Dipping" over the abdomen will elicit a *splashing* wherever both fluid and gas are present in the digestive tract or in the peritoneal cavity. We can feel

Fig. 171.—An enormously distended bladder in a male patient (from the editor's service at the French Hospital).

splashing over the stomach and over the region of the small intestine normally. Over the large intestine, splashing signifies that a diarrhea is either already present or impending. Splashing over the sigmoid region frequently depends upon the overlying small intestine, and cannot be trusted for diagnosis. Over the cecal region, splashing may generally be considered pathologic, and might suggest the possibility of typhoid fever. (Concerning the splashing and swashing in perityphlitis, see p. 376. Concerning the splashing of the stomach, see Stomach Examination, p. 424.) Shaking noises of the abdomen (p. 352), which appear when patients move, can ordinarily be felt as well as heard.

DIAGNOSIS OF INDIVIDUAL VALVULAR LESIONS, OF AORTIC ANEURYSMS, AND OF PERICARDITIS

To appreciate this section the reader should first study the sections upon Cardiac Percussion and Auscultation, and upon Palpation and Inspection of the Cardiac Region.

FOUNDATIONS OF THE PATHOLOGIC PHYSIOLOGY OF VALVULAR LESIONS

EFFECT OF VALVULAR LESIONS UPON THE CIRCULATION; MECHANICS OF COMPENSATION; LAWS GOVERNING THE ALTERATIONS OF SIZE OF THE INDIVIDUAL HEART CHAMBERS IN VALVULAR LESIONS

To understand the symptom-complex of any valvular lesion we must appreciate: the fundamental factors of physical diagnosis (outlined in

the preceding sections), the effect of each individual valvular defect upon the circulation, and the anatomic changes and the modifications of the functions of the individual heart chambers which are produced by the wonderful efforts for compensation. To avoid repetition, the following introduction contains the fundamental factors of the pathologic physiology of valvular lesions:

Any valvular lesion, whether a stenosis or an insufficiency, from the moment of its origin leads to certain alterations in the distribution of pressure upon each side of the affected valve. If the body and the heart itself did not possess a series of powerful compensatory aids to improve this relation of altered pressure, then every serious valvular lesion at its very inception would not only cause serious general disturbances of circulation, but very soon prove fatal. Experience shows that neither is the case. Without compensation the blood in every valvular lesion would be collected behind the diseased valve, and peripherally the blood-mass and the arterial pressure would gradually diminish more and more. The heart's reserve power prevents to a certain extent such a dangerous condition; the heart sections lying behind the injured valve work harder, diminish the blood-stasis, furnish enough blood to the peripheral arteries, and so prevent a dangerous fall of the arterial pressure. The reserve power is utilized in stenosis to overcome the obstacle; whereas in insufficiency it must force more blood forward during the succeeding phase through the injured valve. Rosenbach and Cohnheim produced artificial valvular lesions in animals, and proved that immediately after the onset of a lesion an increase of cardiac work prevented any serious consequences to the circulation. To effect this increased work permanently, anatomic changes in the heart are bound to ensue within a short time. These consist in *hypertrophies* and *dilatations* of the different chambers.

Under the head of *Compensation* we include the entire complex, increased filling and increased work of certain heart chambers, with their resulting dilatation and hypertrophy, *i. e.*, the sum of all those functional and anatomic changes which, in spite of serious lesions of the valvular apparatus, correct the fault up to a certain point, render life possible, and also warrant a condition of circulation endurable to the patient. Compensation, however, does not make the circulation normal, because the pressure behind the valve must be kept abnormally high, so that despite the disturbance the essentials for the circulation may be preserved. What compensation accomplishes is only to keep the pressure in the systemic arteries, capillaries, and veins within the physiologic limits, so that the current rapidity and volume of the circulation are approximately normal, and so that in consequence the most essential bodily functions can be performed without marked subjective symptoms. To fulfil all these requirements, the compensatory changes must naturally prevent the increase of pressure from working backward behind the next valve. Therefore in mitral lesions the most perfect compensation is one which will not increase the blood-pressure nor the volume of blood within the pulmonary circulation. Such patients suffer from dyspnea in case of any unusual demands upon the respiration. (See p. 92.)

This conception of compensation is only a relative one. In this connection another point should be mentioned. In stenoses of the auriculoventricular orifices

and in all insufficiencies[1] compensation does not prevent a stasis in the chambers situated behind the obstacle. The general circulation in these valvular lesions therefore suffers from a blood deficit, because the mass of blood which permanently distends these congested chambers is of no avail. We do not yet know whether in these cases the circulation adapts itself to such a condition by narrowing the remaining vascular system, or whether, in order to make up for the deficit, the blood-mass gradually increases. Unless the latter be the case, the deficit in the circulation would act something like a venesection and be essentially equalized by a narrowing of that part of the vascular system which is not dammed.

Dilatations and hypertrophies of individual heart chambers follow very simple physiologic laws, and from them the cardiac condition in any valvular lesion can be determined.

These laws are as follows:

1. Any heart chamber which suffers an increase of pressure, *i. e.*, has an augmented resistance to overcome only during systole hypertrophies, *i. e.*, corresponding to the greater amount of work, its muscle increases in thickness, without an increase in the size of the cavity (primary hypertrophy).[2] (For certain exceptions see p. 384.)

2. Every heart chamber which suffers an increase of pressure during diastole (*i. e.*, which is more than normally filled during this phase) becomes enlarged (*primary dilatation, dilatation from increased diastole, compensatory dilatation*). In order that the circulation shall be well preserved, it is necessary for the resulting dilated chamber to contract completely or very nearly so. Therefore it must accomplish more work, because, as is well known, the work done during systole equals the product of the systolic volume by the pressure to be overcome. As a result of this increase of cardiac work incumbent upon such a heart chamber its walls must eventually *hypertrophy* (*secondary hypertrophy*). This hypertrophy is apparent either in an increase of thickness of the walls or, perhaps more probably, in a preservation of their normal thickness despite the dilatation.[3]

[1] The stenoses of the arterial orifices behave differently, because they are the only valvular lesions where, during the stage of compensation, there exists no increase of diastolic pressure above the obstacle; in other words, the pressure during systole is increased, but there is no damming behind. There are, however, exceptions even to this—cases where the stenosis from the beginning induces dilatation of the heart chamber above the lesion.

[2] The pathologists designate this kind of hypertrophy of the cardiac wall in which the included cavity is not enlarged as *simple hypertrophy*, in contrast to the so-called *eccentric hypertrophy*, in which the cavity and the thickness of the wall both increase (see the following note). It does not seem easy to explain why an enlargement of the cardiac cavity does not always result as a consequence of the growth of the muscular elements, for it can be proved mathematically, as well as demonstrated experimentally, that the cavity must increase in size coincident with the increase in size of its walls. For example, suppose we place one of the author's glutoid capsules (Deut. med. Woch., 1897, No. 1), filled with some oily substance, in a 2 per cent. solution of muriatic acid and let it stand at an incubator temperature. The capsule-wall will gradually swell, and, since there can be no increase in the internal contents, the surface will become indented, the wall sinking in to fill up the space gained. Now, how can we explain the different behavior in the growth of the heart-wall so that there results a pure simple hypertrophy without any dilatation? Perhaps it is because a growth of muscular fibers in the layers of the myocardium surrounding the cavity is made mechanically impossible by the maximum systolic compression. This compression persists as long as a ventricle for which the requirements for a pure hypertrophy are present (*i. e.*, increased resistance to the systole) is able by means of the reserve power at its disposal to contract completely.

[3] What the author has called *secondary hypertrophy* is the same condition pathologists designate as *eccentric hypertrophy*.

3. Where the conditions for *primary hypertrophy* and *primary dilatation* occur coincidentally, hypertrophy and dilatation of the heart chamber in question may take place entirely independently of each other.

4. In addition to the *primary dilatation* mentioned above (Law 2), a so-called *secondary dilatation* may arise. The latter, for the same reasons as under Law 2, occurs if a heart chamber without any primary increase in its blood-supply be not able to contract fully, and so during diastole suffers an increased pressure, because the blood entering finds a certain amount of blood left there from the preceding diastole. This type of dilatation depending upon an incomplete systole is called a *secondary* or *paralytic dilatation*. It has no compensatory significance, as contrasted with the type of dilatation described under Law 2, which is, as we shall see from examples, of decided value to the circulation, and therefore fittingly called a *compensatory dilatation*.

Dilatations due to incomplete systole are most frequently met with in the so-called compensatory disturbances of heart lesions (see below). Here, despite the variation in their causation, they all possess a common attribute in that they all depend upon cardiac weakness, with the result that systole becomes weaker and the systemic arteries are less completely filled than during compensation. By the appearance of secondary or paralytic dilatations these disturbances of compensation can alter the primary picture of compensated valvular lesions in manifold ways. Such secondary alterations may disappear when the heart has regained its complete power, or they may remain permanent despite the subsidence of the compensatory disturbance, *e. g.*, the secondary dilatation of the hypertrophied right ventricle in mitral insufficiency. The persistence of such secondary alterations may perhaps be explained by the fact that, if a heart chamber has once been stretched by a paralytic dilatation, its recovery is rendered difficult, because the opposition to systolic contraction increases in proportion to the increase in its contents (because the work of a heart chamber in contracting is equal to the product of its pulse volume by the opposed pressure). If this opposition to systole caused by the dilatation reach such a grade that the stretched cardiac muscle, in spite of its secondary hypertrophy, can no longer contract fully and so equalize the dilatation, but is limited to propelling the normal volume of blood from the diastolic position, then the heart chamber in question will finally, to a certain extent, become decidedly dilated with a hypertrophied wall. In this way the paralytic dilatation will persist anatomically fixed, notwithstanding the fact that the compensatory disturbance has receded.

Even without a preceding disturbance in compensation, similar dilatations sometimes affect those parts of the heart which, according to Law 1, should be purely hypertrophied, because they have been subjected, not to greater filling, but merely to increased systolic pressure. The most frequent instance is again the dilatation of the right ventricle in mitral insufficiency, which may occur even without any disturbance in compensation. Such dilatations are, in a measure, related to the paralytic dilatations after a compensatory disturbance which are described above as anatomically fixed. The fact that such a disturbance in compensation does not precede can probably be explained by assuming that the dilatation in these cases begins quite gradually, not from an acute loss of cardiac power, but in consequence of a slow

increase in the obstacle, which has gone too far to permit the persistence of a complete systole, and by further assuming that this dilatation is rendered comparatively harmless by the hypertrophy which develops step by step with it, and becomes at the same time fixed.

Another conception of such primary dilatation of certain chambers of the heart which are simply under higher pressure during the systole and have not been subjected to greater filling is that it is a compensatory phenomenon. The ventricle subjected to an excessive systolic pressure reaches a greater degree of efficiency when its musculature is stretched, just as a skeletal muscle gains in power with an increase in the distance between its two extremities or, better, with an increased initial tension. This is, however, true only up to a certain maximum, after which the power of the skeletal muscle diminishes. This phenomenon, as far as it concerns the skeletal muscles, is sometimes known as "Fick's factor." Nevertheless, the author would not venture to claim that in this respect the heart acts in an analogous manner to the skeletal muscles, nor that this explanation is a better one than the preceding. Such an increase of power in the stretched muscle is perfectly reconcilable with the theory that such a dilated chamber is incapable of complete systole. (See p. 383.) For the work done by the stretched muscle depends on the product of the load times the distance through which it is moved. Here the load is the pressure exerted against systole. This pressure is increased, so that the work done by the muscle, or the power exerted by it, is increased, even if the distance through which the load is moved, represented by the degree of closure, is not. Neither is such a theory incompatible to the view that dilatation beyond a certain degree injures the power of the heart muscle. For it has already been stated that if a skeletal muscle be subjected to too great a degree of tension, its power decreases instead of increasing.

After we have reviewed these latter observations we find that we must modify Law 1, for an increased resistance to the systole of a heart chamber can produce a pure hypertrophy of its wall only so long as this resistance does not exceed a certain degree, but as soon as this point is passed, incomplete systole, dilatation, and finally secondary hypertrophy of the dilated heart chamber occur. Perhaps this will explain the peculiarity that in some cases of chronic nephritis we find a pure hypertrophy, and in other cases a hypertrophy with dilatation of the heart.

It has often been questioned whether such heart chambers, enlarged by paralytic dilatation and later anatomically fixed in their dilatation, ever contract again completely in spite of their increased contents, or whether they permanently produce incomplete systoles. An objection to the former of these two possibilities is that, if no stasis occur, provided a circulation be permanently possible, the other heart chambers will be more extensively dilated during diastole in order to receive the excess of the propelled blood, and so they will be obliged to accomplish correspondingly more work during systole, and for this purpose they must naturally be permanently dilated and at the same time hypertrophied. This would finally result in an entirely purposeless enlargement of and in excessive work for the entire heart, and besides in a purposeless increase in the circulation (excessive compensation). It is not possible definitely and absolutely to decide whether such conditions of the circulation can really occur. They are quite opposed to the teleologic conception of the process of compensation. If so, these permanent excessive burdens of the heart which augment with each disturbance in compensation will furnish an explanation for the fact that practically every heart lesion leads, sooner or later, to a definite cardiac insufficiency, even if the causal valvular lesion does not increase.

To decide whether such a heart chamber with fixed paralytic dilatation always contracts incompletely depends very closely upon another question: Does the systole of the heart, under physiologic conditions, always contract completely, or is it sometimes also incomplete? This controversy must, it seems to the author, according to our present knowledge, be answered in the following way: The ventricle contracts completely or almost completely if the obstacles opposed to its systole be normal. It should act in the same way so long as the obstacles to its emptying

are only slightly increased. Aside from the teleologic significance which the latter condition possesses for the preservation of the circulation even under somewhat more difficult conditions, the author sees a clinical demonstration in proof of it in the fundamental Law No. 1, *i. e.*, with a mere systolic increase of work a ventricle will ordinarily merely hypertrophy without any dilatation. As soon as the slightest increase in opposition prevents the ventricle from contracting completely, it must always dilate, *e. g.*, a dilatation of the right ventricle must, therefore, always occur in mitral insufficiency. With more pronounced opposition to its emptying the heart seems to react with a diminished systole (concurred in by Marey,[1] Dreser,[2] Tigerstedt and Johansson,[3] and O. Frank[4]). The question resolves itself, then, into whether we are to consider this latter phenomenon as a physiologic reaction or as a consequence of a pathologic condition—a weakening of the heart. Personally, in agreement with O. Frank and Moritz,[5] the author considers it a physiologic reaction. His reasons are: the skeletal muscles behave quite analogously; the phenomenon is frequently of great teleologic significance for assisting the heart and the arteries with high blood-pressure; and it has been experimentally demonstrated that such a heart, as soon as the opposition has been reduced, recovers itself immediately and contracts again completely. If we believe that incomplete systoles occur physiologically, it seems perfectly conceivable and entirely within physiologic facts that a cardiac chamber enlarged by paralytic dilatation permanently contracts incompletely.

A certain number of autopsies upon patients with valvular lesions seem to argue against the above-mentioned laws. We must remember, however, that the relations of size of the chambers in the heart of the cadaver differ essentially from those in the living heart, because the phase in which each cardiac chamber is paralyzed (systolic, diastolic arrest) is of especial significance. The degree of rigor mortis of the heart is very rarely heeded at autopsy, although it would be a valuable study to determine the time of onset of the heart-muscle rigor and its influence upon the size of the heart chamber. Moreover, we have no right to compare the relations of the heart of valvular disease at autopsy with the relations of the compensated valvular lesion, because disturbances of compensation usually affect patients with valvular disease some little time before their death, and so the relations of the size of the heart may be very much changed. We will mention this again in the special description of individual valvular lesions.

In reality, therefore, in order to determine the relations of size of the individual heart chambers during good compensation we should utilize only autopsies upon patients with valvular lesions who have died suddenly from some intercurrent trouble, and not those upon patients whose death is directly dependent upon their heart lesion. Even in the former the autopsy finding is not actually and necessarily the same as during life.

It is doubtful whether the Röntgen rays will furnish us more trustworthy results about these relationships.

Compensatory anatomic alterations of the heart are usually permanent, because the valvular lesion itself rarely improves and because life depends upon the maintenance of compensation. Compensatory changes may increase in the course of years, because valvular lesions are often progressive. Where the valvular lesion itself is capable of retrogression, the compensatory changes, too, may retrograde to a slight extent or even completely disappear. These are extremely rare cases.

[1] La circulation du Sang, 1881.
[2] Arch. f. exp. Path. u. Pharm., vol. xxiv.
[3] Skandinav. Arch. f. Physiol., 1889, vol. i.
[4] Zeit. f. Biol., vol. xxxii.
[5] Deut. Arch. f. klin. Med., vol. lxvi.

Dilatations and hypertrophies proceed in accordance with the necessity which occurs, and this necessity can be perfectly explained by studying the above-mentioned laws.

COMPENSATORY DISTURBANCES

A valvular lesion, thanks to the so-called compensatory changes, the hypertrophy and dilatation of individual heart chambers, may for years produce no marked symptoms, but sooner or later the general circulation will be affected more or less decidedly, because compensatory contrivances fail. We then speak of "disturbances in compensation." The causes of these disturbances may be, on the one hand, an increase in the opposition to the circulation produced by the valvular lesion, or the appearance of new circulatory obstacles (arteriosclerosis, nephritis); or, on the other hand, an injury to the heart muscle, which recent investigations have taught us not infrequently depends upon inflammatory alterations of the heart muscle, and which in valvular lesions is frequently produced quite gradually. The same process goes on similarly in other circulatory obstructions which do not depend upon an injured valve. For a long time they also may remain compensated by the hypertrophy of the heart sections above until finally disturbances in compensation ensue here as well.[1] All cases of compensatory disturbance depend upon a disturbance in the favorable relation between the circulatory obstacles and the cardiac power, either an absolute diminution of cardiac power or a relative diminution of the latter in proportion to an increasing obstacle. This condition is exhibited by a diminution of the systoles of all or of individual heart chambers. The heart begins to work with an increasing amount of residual blood in all or in a certain one of its chambers. We shall mention under Individual Valvular Lesions how the relation of the size of the heart is affected by secondary or paralytic dilatations. General stasis ensues in consequence of diminished systoles. If the weakened condition affect the right heart more than the left, the stasis will be localized more in the systemic than in the pulmonary circulation, and vice versâ. Thus, the clinical picture will vary. Compensatory disturbances have, however, considerable uniformity despite the most varied obstacles to the circulation, and they are equally significant

[1] A hypertrophied heart, even under the best conditions, while it may satisfy all ordinary demands upon it, often fails under some extraordinary demand. In other words, even a well-compensated heart lesion, always and under all circumstances, implies a loss of power. This arises from the fact that the hypertrophy is due, not to any increase in the number of muscle-fibers nor, generally, in the contractile substance, but always only to a thickening of the fibers by an increase of the so-called sarcoplasm (Albrecht, Der Herzmuskel, Berlin, 1903). According to Albrecht, the sarcoplasm is merely the nutritive part of the muscle-fibers. The hypertrophied chamber, therefore, gains no absolute increase of power, but is merely enabled, by the extra supply of sarcoplasm, to maintain for a longer time its increased activity. Albrecht considers that this increased activity is not due to the hypertrophy at all, but is merely the reserve force possessed by a normal heart. But this reserve force can be used permanently only by a hypertrophied chamber, which is able to supply an extra quantity of sarcoplasm. The fact that a hypertrophied heart easily gives out when extra work is put on it, is thus readily explained. The power of such a heart is at best normal, and a greater or less part of this power has already been consumed in overcoming the resistance to circulation, the cause of the hypertrophy. This fraction of the total force is, therefore, no longer available for meeting unusual demands upon the heart.

whether the diminution of heart power proceeds from the left or from the right heart. Only in rare individual cases do these disturbances vary decidedly. This uniformity probably depends upon the fact that the coronary arteries are injured as much in paralysis of the right as in paralysis of the left heart, so that the entire heart finally shares in the paralysis. This usually uniform clinical picture of compensatory disturbance may be described as follows: The filling of the systemic capillaries diminishes. The distention of the veins and the venous pressure increase. The circulation is slowed by diminution in the blood-supply. Cyanosis and dyspnea ensue. Edema and other dropsical accumulations are added. The urinary excretion is diminished and the urine frequently contains albumin. The causes of these appearances are discussed in the sections on edema, dyspnea, cyanosis, amount of urine, and albuminuria. The pulse frequently varies; it is very often accelerated, as if the heart attempted to overcome to some extent its fault of incomplete contraction by great frequency of contraction. This depends probably upon accelerator stimulation, due to the insufficient circulation. The heart action is frequently very irregular and produces the impression of overstimulation. This is probably due to a disturbance in the automatism of the damaged heart. Very pronounced irregularity has been designated quite properly delirium cordis. Neither great rapidity nor irregularity of the pulse necessarily accompanies compensatory disturbances. Like the other symptoms, one or the other of them may be lacking or very much less pronounced. The single constant factor in compensatory disturbances is the diminished cardiac power and the insufficient systole. Quite an important diagnostic sign of disturbed compensation in a valvular lesion with an audible murmur is that this murmur may become fainter and perhaps inaudible on account of the diminution in the current rapidity within the heart. On the other hand, a dilatation of the ventricle caused by the disturbed compensation may produce a murmur where one was not audible before, or bring one out very much more distinctly, due to a relative insufficiency of the auriculoventricular valve (p. 329 et seq.), which is superimposed upon the original lesion. This subject has already been discussed under Cardiac Murmurs. From evident reasons, the heart tones are frequently weaker in disturbed compensation. In patients with disturbed compensation we sometimes find a relatively tense pulse (*i. e.*, high arterial pressure), which would seem to argue against our explanation that compensatory disturbances depend essentially upon insufficient cardiac power. As a matter of fact, the difficulty vanishes when we remember that the work of the left ventricle does not depend merely upon the arterial pressure, but is measured by the product of the arterial pressure by the volume of blood emptied during systole, and that with marked arterial resistance even a very small systole may produce high arterial pressure. The author calls such a condition "high-pressure stasis,"[1] in contrast with the more frequent "low-pressure stasis," where arterial pressure is diminished by the disturbed compensation. "High-pressure stasis" occurs especially in circulatory disturbances associated with arteriosclerosis or chronic nephritis or in stasis from any cause, in case the tone of the vessels is increased by dyspnea.

[1] See Sahli, Herzmittel und Vasomotorenmittel, Cong. f. inn. Med., Berlin, 1901.

INDIVIDUAL VALVULAR LESIONS

The alterations in size of the different heart chambers (dilatations and hypertrophies) which occur in individual valvular lesions will be explained perfectly by a thorough comprehension of the laws which have been discussed in the preceding pages concerning the origin of compensation and the disturbances of the same. For the sake of brevity only the number of the law which explains the hypertrophy or dilatation will be mentioned in the text. (See p. 382 et seq.) The reader will find that his comprehension of these laws will be facilitated by studying the hydraulic diagram given at the beginning of each description. He will find represented there the alterations in pressure which the valvular lesion produces upon each heart chamber. The explanation of the signs employed in these diagrams is given with Fig. 172. The reader should consult pages 309 to 340 in order to understand the diagrams representing the results of physical examination in each valvular lesion, and he should recall (p. 217 et seq.) that the blue represents the superficial, the red the deep cardiac, dulness. A cross (×) is used to designate the point upon the skeleton for the percussed boundaries. The shaded wedges represent the murmurs, and their thickness the intensity of the murmur. Near the blunt end of the wedge the sign > represents a diminuendo murmur; the sign < represents a crescendo murmur. The tones at the apex of the heart and over the tricuspid valve are represented by the signs ⊥ ⌣; while over the base of the heart (over the great vessels) the tones are represented by the signs ⌣ ⊥. The phase of the murmur is determined by its position, as compared with the tones. Accentuation of the tone is represented by an accentuation of the sign.

VALVULAR LESIONS OF THE LEFT HEART

The valvular lesions of the left heart are much the most frequent. (Congenital heart disease is not included.) In any given case, therefore, the diagnosis will be facilitated by the rule that wherever a valvular lesion appears after birth, as a result of joint rheumatism or arteriosclerosis, we should think first of a left-sided lesion. On the contrary, in congenital cardiac disease we think first of right-sided valvular lesions.

MITRAL INSUFFICIENCY

The essential fault in *mitral insufficiency* (Figs. 172 and 173) consists in a systolic regurgitation of blood into the left auricle. This regurgitation depends upon the imperfect closure of the mitral valve and gives rise to a systolic murmur. It is the most frequent of all valvular lesions. The regurgitation increases the pressure in the auricle enough to dilate it (Law 2). The increased pressure in the auricle is transmitted back through the entire pulmonary circulation. The pulmonary semilunar valves, however, are shut during diastole, so that the right ventricle does not suffer from the increased pressure at this stage. But the increased pulmonary pressure acting to augment the work of the right ventricle during systole necessitates its hypertrophy (primary hypertrophy) (Law 1, p. 382). Dilatation of the left auricle is responsible for its own secondary hypertrophy (Law 2). But there is another especially important element. The left ventricle receives more blood during its diastole than normally because the left auricle is overfilled;

hence it becomes primarily dilated (Law 2) because the pressure within it is increased during diastole. This dilatation leads in turn (Law 2) to a *secondary hypertrophy* of the left ventricle. The reason for the left ventricular dilatation is plainly compensatory; because, despite the fact that a part of its blood is regurgitated into the auricle, its increased capacity enables the arterial system to be completely filled.[1]

In a well-compensated mitral insufficiency the systemic circulation is practically normal. The pulse is not at all small, as has often been stated, and the only striking disturbance which persists during compensation, even of a severe case of mitral insufficiency, is a more or less pronounced *dyspnea*, which ensues because the lungs are overfilled with blood. (See pp. 92 and 381.)

With this the series of compensatory changes in mitral insufficiency is complete. Clinically (Fig. 173), the lesion is recognized by a systolic murmur, generally heard with maximum intensity at the apex of the heart, but, under certain circumstances (see p. 333 et seq.), with its

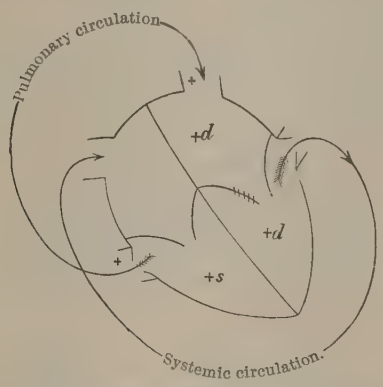


Fig. 172.—Hydraulic diagram of mitral insufficiency: +, Increased pressure; +*s*, increased systolic pressure; +*d*, increased diastolic pressure; +*ds*, increased systolic and diastolic pressure in the heart chambers within which the signs appear. Hence, a heart chamber marked with +*s* hypertrophies primarily; one with +*d* dilates primarily; and one with +*ds* both dilates and hypertrophies primarily.

maximum at the base. This murmur may even overpower or obliterate the systolic mitral tone. Sometimes we can feel a thrill as well as hear a murmur. The primary dilatation of the left ventricle and left auricle can be demonstrated by percussion (frequently by palpation). Simple or pure hypertrophy of the right ventricle cannot ordinarily be appreciated by percussion (p. 242); but the increased pressure in the pulmonary circulation which produces this hypertrophy of the right ventricle is generally evident from an accentuation of the second pulmonic tone (p. 317), sometimes from the increased pulsation, or from the shock of the pulmonary valve closure, visible or palpable in the region of the pulmonary artery (p. 368). The diagnostic significance of the pulmonary second accentuation is, however, frequently overestimated. Not

[1] Theoretically, a very slight, practically negligible, deficit in the filling of the entire system of blood-vessels must necessarily ensue, because an extra amount of blood is required for the increased filling of the pulmonary circulation, of the left auricle, and of the left ventricle.

infrequently it fails to appear, for there are many cases where the compensatory power of the right ventricle is not sufficient to produce it, or cases of a mild degree of insufficiency, where the increased pressure is slight; and, finally, cases where, before the appearance of the mitral insufficiency, the pulmonic second was physiologically weaker than the aortic second. In contradistinction to the diastolic murmur of aortic insufficiency (see p. 397), it is worth remembering that the murmur of mitral insufficiency is heard with less intensity when the patient is standing than when lying down. This is very likely due to the action of gravity opposing the regurgitation. In fact, a faint mitral insufficiency murmur can frequently be heard only in the recumbent posture.

The above-mentioned signs are ordinarily noted in an early case of mitral insufficiency. Sooner or later, however, disturbances of

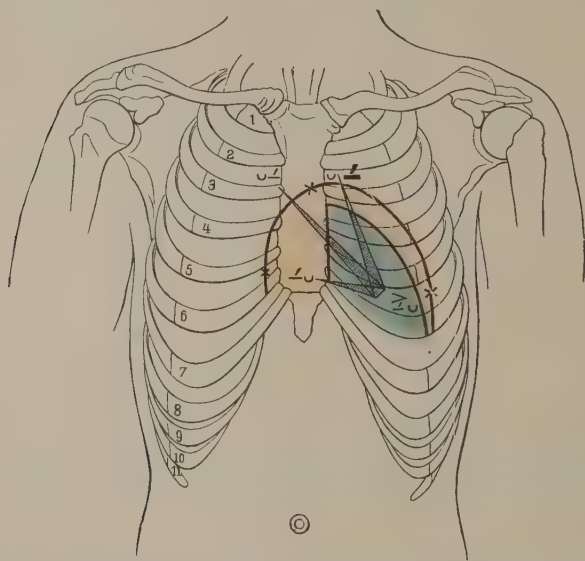


Fig. 173.—Diagnostic diagram of mitral insufficiency. (The signs are described upon p. 388.)

compensation are bound to appear. They ordinarily begin in this way: The right ventricle can no longer completely contract, and therefore dilates (paralytic dilatation, Law 4); as a consequence the accentuation of the second pulmonic disappears, the left auricle and the left ventricle in turn receive less blood, and the filling of the systemic arteries and capillaries diminishes. This last danger-signal is still more marked when, from the same cause, the left ventricle begins to weaken. All the other appearances of disturbed compensation described above can be added to the lack of arterial filling until, under the influence of rest or cardiac tonics, compensation is again established. The heart power then increases. The right ventricle again empties itself completely and returns to its condition of pure or simple hypertrophy. But ordinarily during the course of reëstablishing compensation the dila-

tation of the right ventricle becomes anatomically fixed by the development of a secondary hypertrophy, *i. e.*, by the addition of layers of new muscular tissue (p. 386). This is permanent and can be demonstrated by percussion. (See p. 384 in reference to the completeness of the contraction of this permanently dilated right ventricle.) With the reëstablishment of compensation the severe circulatory disturbances completely disappear.

The right ventricle may become dilated and hypertrophied in a similar way even without disturbance of compensation depending upon the conditions described upon p. 383.

The answer to the question as to whether or not the permanent dilatation of the right ventricle in mitral insufficiency has a compensatory significance depends upon whether or not we assume that the mechanism of the Fick's factor (p. 384) plays a part in improving the function.

(See p. 149 in regard to the characteristics of the pulse in mitral insufficiency; p. 353, in regard to the presence of a pulmonary pulse; p. 228, in regard to the depth of the lung borders from pulmonary stasis; p. 381, in regard to the character of the respiration; p. 318, in regard to the occasional disappearance of the mitral tone or both tones of the left heart; p. 337, in regard to the difference between a mitral and an aortic systolic murmur; p. 336, in regard to the occurrence of a prediastolic murmur, and p. 322, in regard to a splitting or doubling of the second tone.)

MITRAL STENOSIS

In mitral insufficiency the obstacle to the circulation is effective during systole; but in mitral stenosis, a comparatively frequent valvular lesion, the obstacle acts during diastole of the left ventricle. To understand

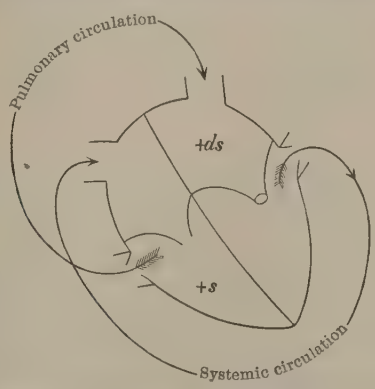


Fig. 174.—Hydraulic diagram of mitral stenosis. (See Fig. 172 for the explanation of the signs.)

what follows we should remember that the ventricular diastole can be subdivided into two intervals in relation to the auricle (Fig. 174). During the first part of the ventricular diastole the auricle is passive; the blood, under the influence of the pressure remaining from its course through the pulmonary circulation, flows into the left ventricle without the aid of the auricle. In mitral stenosis, however, an obstacle pre-

vents this emptying of the auricle; the pressure therein increases, and, the blood collecting, stretches the auricular walls, which are ordinarily relaxed at this period. The first result of mitral stenosis upon the heart (Law 2) is therefore the dilatation of the left auricle. During the second part of ventricular diastole the auricular systole comes into action, and on account of the stasis behind the stenosed mitral valve it has to propel an increased amount of blood, and in addition overcome the obstacle at the mitral valve. As a result (Laws 1 and 2) a hypertrophy of the dilated left auricle supervenes. We might imagine that (without help from the right ventricle) the increased power of the left auricle could effect the compensation. But experience has shown us that this is not the case, and that hypertrophy of the right ventricle belongs as much to mitral stenosis as to mitral insufficiency. Despite the increased work of the left auricle there remains, therefore, an increased

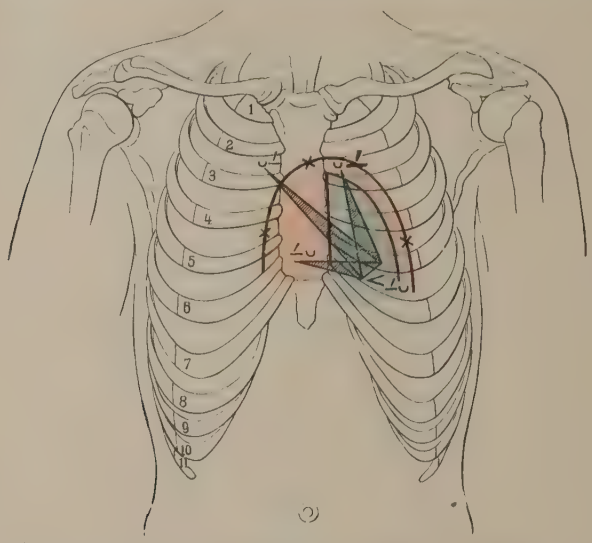


Fig. 175.—Diagnostic diagram of mitral stenosis. (See p. 388 for the explanation of the signs.)

task for the right ventricle. The explanation is probably that the left auricle does not grow to be strong enough both to expel completely its increased content and to overcome the mechanical obstacle of the narrowed mitral valve.[1] This is not to be wondered at when we consider the slight muscular power of the auricle; and, as a matter of fact, autopsies show no very striking hypertrophies of the auricle. Assuming, then, that in mitral stenosis the left auricle cannot completely empty itself, and so is continually laboring with residual blood, it happens, naturally, that during auricular diastole the blood from the lungs does not flow into an empty, but into an already partially filled, left auricle. This is of equal significance to the pulmonary circulation with an increased resistance present during auricular diastole or ventricular sys-

[1] Perhaps the same laws in regard to the completeness and incompleteness of contraction apply here as to the ventricle. (See p. 384.)

tole. There are no valves between the auricle and the lungs, and the distention of the auricle destroys any valvular closure, such as is assumed by physiologists to act through a ring-shaped narrowing of the orifices of the pulmonary veins; hence it is easy enough to understand that the contraction of the left auricle must drive back a part of the blood stagnating in the auricular chamber into the lungs and part through the narrowed mitral valve.[1] The increased resistance in the pulmonary circulation persists until the ventricular systole occurs, and can be overcome only by the hypertrophy (primary) of the right ventricle (Law 1). Thus, the hypertrophy of the right ventricle in mitral stenosis enables compensation to be effected by producing a continuous diastolic flow through the stenosed mitral valve. It presupposes an elastic tension of the pulmonary vessels, so that the systolic power of the right ventricle is transmitted through the lung into the left auricle. The effect upon the left auricle and the pulmonary vessels can be likened to the action of a wind hose. Despite its complexity, this supposition alone seems to explain that the systole of the right ventricle aids in producing compensation, although the obstacle is diastolic.[2] The conditions are much simpler in mitral insufficiency; for here, as a direct result of the regurgitation, both ventricles are working directly at variance, making it perfectly clear why the right ventricle must do more work.

There is no necessity for a dilatation of the hypertrophying right ventricle in mitral stenosis, any more than in mitral insufficiency, because, in either case, so long as the pulmonary semilunar valves close perfectly, there is no increase of right ventricular pressure except during systole (Law 1). Nevertheless, a dilatation may also occur in mitral stenosis, and then it is produced in the same fashion as in mitral insufficiency. (See p. 390.) In regard to its compensatory significance, see p. 384. Stenosis of the mitral valve furnishes no reason for any change in the left ventricle. In a well-compensated mitral stenosis the left ventricle evidently does not show concentric atrophy, as is sometimes contended, because our conception of good compensation is not compatible with the supposition, necessarily included in such a contention, that the diminished left ventricle forces decidedly less blood than normally into the systemic arteries.[3]

We not infrequently see at the autopsy table a case of mitral stenosis with a large right and a small left ventricle. The reason is either that the lesion could not be compensated, on account of the extreme degree of the obstruction (essential stasis[4]), or that the patient died during a disturbed compensation, in which the incomplete systole of the

[1] The fact that a considerable portion of the blood is driven backward instead of forward by the auricular contraction also explains the absence of dilatation of the left ventricle, in spite of the increase in the pulse volume of the left auricle.

[2] This passive elastic function, in which the propelling force is traced back to the right ventricle, is in reality a normal function of the left auricle and the pulmonary vessels, since during the first part of the ventricular diastole the blood flows into the left ventricle mainly on account of the excess of pressure which is left over from the lungs.

[3] The deficit which the systemic circulation suffers in consequence of the collection of blood in the left auricle and in the lungs is of little importance to the left ventricle during the stage of compensation, because the vessels of the greater circulation possess a capacity for adapting themselves to varying degrees of fulness. Perhaps the deficit is cared for by an increase of the blood-mass. (See p. 382.)

[4] The reader is referred to the author's paper: "Herzmittel und Vasomotorenmittel" (Cardiac and Vasomotor Remedies), Cong. f. inn. Med. at Berlin, 1901.

right ventricle occasioned a paralytic dilatation of its own chamber, and consequently an imperfect filling of the left ventricular cavity.

This paralytic dilatation of the right ventricle may remain fixed even after the disturbed compensation has been adjusted, and an enlarged and hypertrophied right ventricle may result permanently, just as in mitral insufficiency. Even without actual disturbance of compensation the same result may, under some circumstances, be accomplished by the causes mentioned upon p. 383. Whether such a dilated and hypertrophied right ventricle then contracts incompletely or completely is not certain. (See p. 384.) The latter would have some effect upon the other heart chambers, for the left auricle and the left ventricle would then contain more blood than normally and the left ventricle would also be dilated. In this way we might explain cases of pure mitral stenosis which show a dilatation of the right, as well as of the left, ventricle. But such a supposition cannot be accepted without hesitation, because it supposes that the diseased mitral stenotic heart would finally perform a greater systolic effort than the healthy heart. And this is not only *a priori* improbable, but it is not in any way supported by the character of the pulse. So in mitral stenosis, where we meet with a dilatation of the left ventricle, we assume either a simple paralytic dilatation from a final paralysis of the left heart, or, with a coincident hypertrophy of the left ventricle, the coexistence of mitral insufficiency. The latter may escape anatomic demonstration and, if there be no systolic murmur, even clinical confirmation.

Mitral stenosis (Fig. 175) will produce a dilatation of the left auricle (see pp. 246 and 247), which can be demonstrated by percussion; but the hypertrophy of the right ventricle, unless associated with dilatation, ordinarily escapes such clinical demonstration. In later stages mitral stenosis may be associated with an appreciable increase of the heart dulness to the right as well as to the left. The enlargement to the left may, in exceptional cases (see above), be due to a true dilatation of the left ventricle; but ordinarily it is the dilatation of the right ventricle which pushes the heart and the apex-beat to the left. (See pp. 357, 244 et seq.)

In a case of mitral stenosis we generally hear a diastolic murmur with a presystolic accentuation or merely a presystolic murmur at the apex; frequently we can also feel it as a presystolic thrill. (In regard to the mode of production of this murmur and its significance see p. 335 et seq.; in regard to the peculiarity of its localization see p. 333; in regard to the presystolic mitral murmur of aortic insufficiency see p. 397.) The second pulmonic tone is generally accentuated in mitral stenosis in consequence of the increased pressure in the pulmonary circulation and the hypertrophy of the right ventricle. The value of this sign for the diagnosis of mitral stenosis has, however, often been overestimated. (See p. 317.) If compensation be disturbed, the accentuation may disappear. The normal second pulmonic tone is often weaker than the normal second aortic tone, so that a pathologic accentuation of the former is frequently not apparent to the examiner. And, finally, with a mild degree of mitral stenosis, the increase of pressure in the pulmonary circulation may be insufficient to produce a plain accentuation of the second pulmonic. (See p. 318 et seq. in regard to an apparent or actual accentuation of the mitral valve tone.)

We frequently hear a splitting or doubling of the second tone (see

p. 322 et seq.), and occasionally a presystolic or diastolic tone, due to an imperfectly opened mitral valve. (See p. 324 et seq.)

During quiet cardiac action sometimes the only auscultatory sign of mitral stenosis is a triple rhythm, the third tone of which is furnished by the presystolic tone. Besides, it is well to remember that mitral stenosis is more liable than any of the other valvular lesions to run its course without giving rise to a murmur. (See p. 330.)

In regard to the character of the pulse of mitral stenosis see p. 149; in regard to the character of the respiration see pp. 92 and 381; in regard to the presence of a pulmonary pulse see p. 353; in regard to the deep position of the lung borders on account of pulmonary rigidity see p. 227 et seq.

AORTIC INSUFFICIENCY

Aortic insufficiency—imperfect closure of the aortic valve (Figs. 176 and 177)—is, next to mitral insufficiency, the most common valvular lesion. Its mechanism is the one most readily comprehended by the

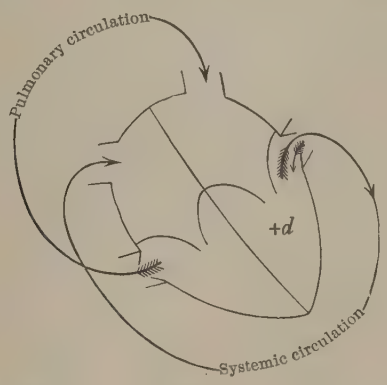


Fig. 176.—Hydraulic diagram of aortic insufficiency. (Compare Fig. 172 for explanation.)

beginner. The fault is that during diastole (Fig. 176) the blood rushes back into the left ventricle through the imperfectly closed semilunar valves, and so gives rise to the characteristic diastolic murmur (see below). Without compensation the mechanical effect upon the circulation would be that the aorta, deprived of part of its blood during diastole, could not fill the arteries and keep up the pressure. Compensation prevents such a result in the following way: The regurgitating blood enters the diastolic relaxed left ventricle. This chamber is at the same time receiving blood through the mitral valve. Its walls have, therefore, to endure an increased pressure during diastole, and hence become dilated (p. 382 et seq., Law 2). In virtue of its reserve power the left ventricle still contracts itself completely, and naturally sends an increased volume of blood into the aorta. But it cannot continually perform this extra work without hypertrophy (Law 2). As soon as hypertrophy takes place, the valvular lesion is compensated, and, for the time being, harmless. Then, at every systole, the aorta receives more blood than normally, and the loss through regurgitation is not significant. So

one sees in this lesion, as in mitral insufficiency, that the dilatation of the left ventricle is primary, and that it is essential to the accomplishment of compensation. Therefore primary dilatation and secondary hypertrophy of the left ventricle are an essential result of aortic insufficiency (Fig. 177). Frequently a diffuse dilatation of the aorta, which depends upon its being stretched by the increased power of the systole, goes hand in hand with the dilatation of the left ventricle. This aortic dilatation may become evident in the appearance of a pulsation and an increased dulness in the upper intercostal spaces to the right of the sternum (Fig. 143). It is liable to be confused with a sacculated aortic aneurysm. (See p. 413.) The right ventricle takes no part in compensating for an aortic insufficiency. But as soon as disturbance in compensation arises, as soon as the left ventricle is unable to perform its

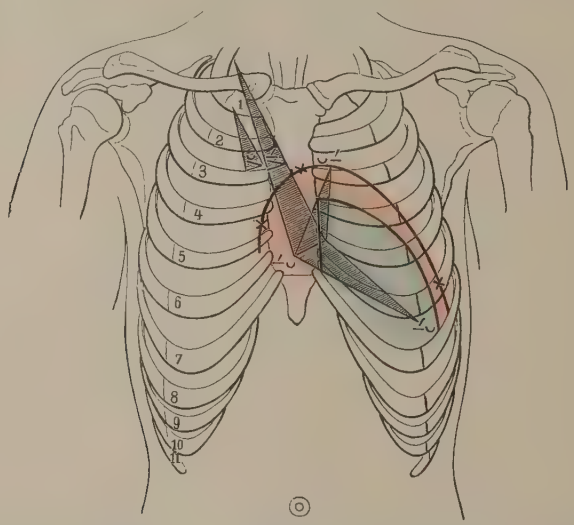


Fig. 177.—Diagnostic diagram of aortic insufficiency. (See p. 388 for an explanation of the signs.)

increased work perfectly, so that during systole it is incompletely emptied, then the residual blood within its cavity prevents a complete emptying of the left auricle, and, just as in mitral stenosis, this reacts upon the pulmonary circulation and the right ventricle. If such a paralysis of the left ventricle occasion a considerable dilatation of its chamber, a relative mitral insufficiency will also appear, and, in the well-known way, react upon the pulmonary circulation and the right ventricle. This reaction upon the pulmonary circulation, which, according to our discussion above, does not depend entirely upon the occurrence of a relative mitral insufficiency, but which can sometimes be caused by the residual blood in the left ventricle, explains how failure of the left ventricular power in aortic insufficiency finally produces the ordinary picture of disturbance of compensation, with cyanosis, dyspnea, edema, etc., just as in the mitral lesions. The disturbance of

compensation may be repaired; and then, depending upon the individual peculiarities of the case, the right ventricle either regains its normal size, or else, if a relative mitral insufficiency (see p. 383 et seq.) persist on account of the permanently dilated (see p. 383) left ventricle, it may remain permanently hypertrophied, or both hypertrophied and dilated. Such a permanent dilatation of the right ventricle, supposing it contracted itself completely, would produce secondarily a further enlargement of the left auricle and ventricle (excessive compensation?). (See p. 384.)

The most important of the physical signs of this valvular lesion (Fig. 177) is a diastolic murmur audible at the aortic area and over the sternum. (See p. 332, 2.) The murmur is sometimes plainly transmitted into the carotids, and is usually more distinctly heard in the standing than in the recumbent posture, because gravity favors the regurgitation. A weak murmur of aortic insufficiency (contrasted with that of a mitral insufficiency, p. 390) is, therefore, oftentimes audible only while the patient is standing.[1] The second aortic sound may be absent; again, it may be unaffected if the aortic valves be not much diseased, or it may even be accentuated, in consequence of the increased systolic filling of the aorta; but, more frequently, on account of the damaged aortic valves, it is diminished or even disappears. In most cases of aortic insufficiency a systolic murmur can also be heard over the aorta. According to one hypothesis, this systolic murmur depends upon a roughness at the aortic valves, due to endocarditis or atheroma, which affects the blood-current during systole, although there is no actual stenosis (p. 328, 2). According to another hypothesis, the systolic murmur results from the diastolic regurgitating stream clashing with the systolic stream. According to a third hypothesis, it is the result of the increased rapidity of expulsion of the blood from the more powerful systole (p. 327). However this may be, it is well to be cautious in making a diagnosis of aortic stenosis from the presence of a systolic murmur heard over the aorta in a case of aortic insufficiency unless there are other signs of stenosis. An especially rough or musical murmur speaks with some probability for the existence of an aortic stenosis; but the deciding point is the character of the pulse. If there be an actual aortic stenosis,—that is, a mechanical narrowing,—the pulse will possess, more or less plainly, the characteristics of the *pulsus tardus*. (See p. 115 et seq., p. 144.) See p. 340 in regard to the presence of a doubled maximum diastolic and systolic murmur, *i. e.*, one heard very plainly both over the aorta and at the apex. A complicating mitral insufficiency or stenosis is often wrongly diagnosticated from such signs.

Austin Flint[2] described in aortic insufficiency a presystolic murmur audible over the auscultation area of the mitral valve. He explained it in this way: The regurgitating stream from the aorta spreads out the curtain of the mitral valve just as the presystolic stream from the left auricle is passing through this valve into the left ventricle. Hence the mitral curtain cannot be completely opened, and a sort of functional mitral stenosis results. This produces the presystolic murmur. This explanation does not seem to the author sufficiently proved by the postmortem findings; nevertheless, it deserves diagnostic attention. A certain differentiation of this condition from the combination of an aortic insufficiency

[1] [A very faint murmur of aortic insufficiency can sometimes be appreciated by the ear against the chest when it is not audible through the stethoscope.—Ed.]

[2] [Flint's murmur, first described in Manual of Auscultation and Percussion, Austin Flint, third ed., 1883, p. 231.—Ed.]

with an organic mitral stenosis must be very difficult. Certainly such a functional origin of a pronounced presystolic murmur is rare, so that the diagnosis of a mitral stenosis complicated with aortic insufficiency is not so difficult. [The "Flint murmur" is, in my experience, by no means rare.—Ed.]

Further important diagnostic signs of aortic insufficiency are: the *pulsus celer* (pp. 115 and 144) and a series of signs depending upon it, which have been explained above; a *capillary pulse* (p. 190 et seq.); the *single and double arterial tones* (p. 348); the *Duroziez double murmur* (p. 348 et seq.), triple tones and autochthonous systolic murmurs in the carotid; the rare appearance of the *penetrating venous pulse* (p. 197 et seq.); the rare *arterial liver pulse* (p. 198), and the Oliver-Cardarelli sign. All these signs are, of course, most plainly marked during good compensation; less plainly during disturbed compensation. They are not all equally plain. The reader is referred to p. 177 et seq. for the advantages of employing the *absolute* sphygmogram for the exact sphygmographic demonstration of the pulsus celer. The broad, dome-like apex impulse (see p. 360) is quite characteristic of aortic insufficiency and corresponds to the rounded configuration of the cardiac apex peculiar to this valvular lesion.

During disturbance of compensation in aortic insufficiency the character of the pulse still seems exceptionally well preserved despite the poor circulation. This depends, in the first instance, upon the fact that, even with poor filling of the arteries, the pulse does not lose its character of *pulsus celer*, which would naturally produce the impression of a relatively good pulse. Besides, measurements of the direct pressure by means of the sphygmomanometer show that, with this valvular lesion, the systolic pressure (see pp. 115 and 158 et seq.) can be high despite disturbance in compensation. This only apparently contradicts our statement above in regard to the characteristics of disturbance of compensation. For aside from the fact that disturbances of compensation when the arterial resistance is decided are not necessarily associated with a low blood-pressure (see p. 387, high-pressure stasis), we must not forget that the systolic pressure in this valvular lesion should be considered a much less exact measure of the mean arterial pressure than under ordinary circumstances, because a considerable portion of the systolic pressure is, on account of the regurgitation, of no use to the circulation. And so it happens that an abnormally high systolic pressure, for perfect compensation in aortic insufficiency, is in reality essential to establish a mean normal pressure in the capillaries. And then even in disturbed compensation the absolute systolic pressure will almost always be normal or above normal. Moreover, the pulse of aortic insufficiency, having the character of pulsus celer, it will be felt a longer time than normal on the proximal side of the pelotte of the sphygmomanometer and thereby cause an overestimation of the systolic pressure.

AORTIC STENOSIS

Aortic stenosis (Figs. 178 and 179) causes an obstacle to the left ventricular systole. The left ventricle overcomes this obstacle at first by means of its reserve power, and later by the hypertrophy of its walls—ordinarily a pure primary hypertrophy without dilatation (p. 382, Law 1). The hypertrophy of the left ventricle may not be demonstrable clinically, or it may exhibit only an accentuation of the apex impulse (see p. 358 et seq.) without any cardiac enlargement evident to

percussion. (See p. 242.) Sooner or later, however, disturbances in compensation generally occur, and a secondary dilatation of the left ventricle is added to the hypertrophy (Law 4). This dilatation either disappears

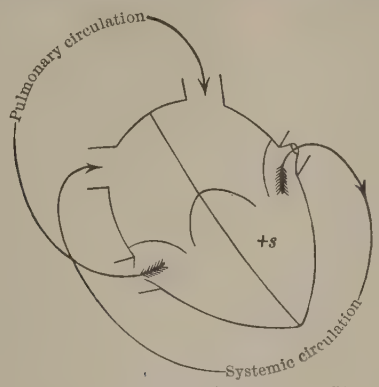


Fig. 178.—Hydraulic diagram of aortic stenosis. (Compare Fig. 172 for explanation.)

when compensation is restored, or may persist as an anatomic change. (See p. 384 et seq.) Such a permanent dilatation (p. 384) sometimes develops without being preceded by a real disturbance in compensation.

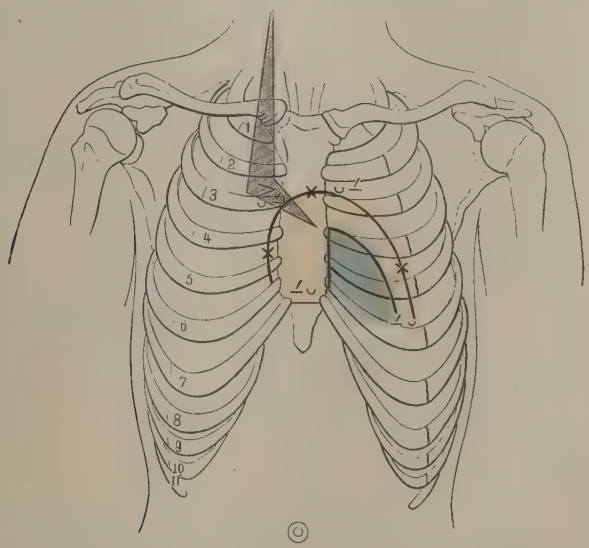


Fig. 179.—Diagnostic plan of aortic stenosis. (For explanation of the signs see p. 388.)

(See p. 384 et seq. in regard to the completeness or incompleteness of contraction of such a permanently, secondarily dilated and hypertrophied ventricle.) It need scarcely be mentioned that, through disturb-

ances in the compensation, an aortic stenosis may produce the same effect upon the pulmonary circulation and the right heart (p. 396 et seq.) as aortic insufficiency.

The physical signs of aortic stenosis are pictured in Fig. 179. Auscultation reveals a systolic murmur, audible over the aortic area in the second right intercostal space, transmitted upward to the vessels of the neck, and sometimes audible over the entire left ventricle. The murmur is also palpable at times, and may even be heard at a distance. It is so constantly loud that the demonstration of a loud systolic murmur argues in favor of aortic stenosis and against an accidental murmur; and, as a matter of fact, the conditions for murmur formation (great rapidity of the current, large volume of the stream) are more favorable in aortic stenosis than in almost any other valvular lesion. The murmur may possess two maximum points (over the aorta and at the apex). (See p. 339.) This may produce the erroneous impression of a complicating mitral insufficiency. The most essential sign of aortic stenosis is the *pulsus tardus,* the presence and peculiarity of which have been explained. (See pp. 115 et seq., and 144.) Very frequently no distinct pulsus tardus exists, and the only abnormality in the pulse is its smallness. (See p. 144.) This latter peculiarity may depend upon so many different causes that it is of no diagnostic value. The absolute sphygmogram is to-day a requisite for the positive demonstration of a pulsus tardus. The tension of this deliberate and small pulse-wave during the stage of compensation is not necessarily low. Often it is not only tardy and small, but also less frequent than normal. Evidently the slowness of the cardiac action essentially lessens the heart's work, and in a high grade of aortic stenosis it is an important condition for the establishment of complete compensation, and is therefore of especial diagnostic significance. Despite the hypertrophy of the left ventricle, the apex impulse is said to be frequently weakened; but this is certainly not always the case. Where such a weakened apex-beat does appear, Gutbrod-Skoda's theory that it is due to a loss of recoil depending upon slowness of cardiac emptying will not satisfy the conditions. For we know that the apex impulse coincides with the closure time of the heart. Hence we must acknowledge that the recoil theory of the heart impulse has been finally disproved. Rosenstein's explanation seems more plausible. He claims that the hypertrophy produces a more rounded left ventricle, and that it is more difficult for such a rounded apex to reach between the ribs, and so the apex impulse is weakened. But, as a rule, the cardiac apex is also decidedly rounded in aortic insufficiency, and yet in this latter lesion the heart impulse is usually quite pronounced. The author considers the causal relation between the weakening of the apex-beat and aortic stenosis has not yet been proved. Besides, many cases of aortic stenosis exhibit the accentuated slowly heaving apex impulse which has been described and explained on p. 359.

There is nothing characteristic about the tones in aortic stenosis. Ordinarily, they persist. Under some circumstances decided weakness of the tones over the entire left heart makes it probable that a mitral insufficiency complicates the aortic stenosis. (See p. 318 et seq.) In this lesion the shape of the cardiac dulness as outlined by percussion may be normal; hence the probability of confusion between the systolic murmur of an aortic stenosis and an accidental murmur from atheroma

or roughness of the aortic intima. The pulse should distinguish the two conditions. Other kinds of accidental murmurs (anemia, fever) are less difficult to diagnose, because their maximum is not usually over the aorta. The author has already emphasized (p. 397) the frequent error of diagnosing a complicating aortic stenosis because a systolic murmur is heard over the aorta in addition to the diastolic murmur in aortic insufficiency. The presence or absence of the *pulsus tardus* should be distinctive in this case as well. To distinguish the murmur of aortic stenosis from that of mitral insufficiency we should carefully locate its maximum intensity and notice the characteristic, although slight, difference of phase (p. 336 et seq.).

VALVULAR LESIONS OF THE RIGHT HEART

In the diagnosis of valvular lesions of the right side of the heart it is important to remember that they are most frequently congenital lesions, and that they rarely originate during extra-uterine life; this is exactly the reverse of left-sided lesions. Nevertheless, acquired right-sided valvular lesions are not quite so rare as is sometimes claimed. When they do originate after birth, they are most frequently complications of coexistent left-sided lesions.

TRICUSPID INSUFFICIENCY (Figs. 180 AND 181)

As a relative insufficiency complicating left-sided valvular lesions, this lesion occurs quite frequently; but as a true anatomic valvular change, it is rare except in congenital heart disease. The weak right auricle is all that exists behind the tricuspid value to compensate the

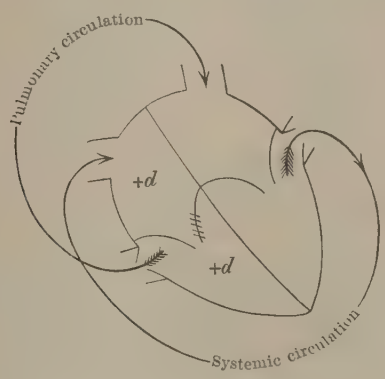


Fig. 180.—Hydraulic diagram of tricuspid insufficiency. (For explanation see Fig. 172.)

disturbance. Its compensatory power is naturally limited, so that the disturbance to the circulation is more serious than in mitral insufficiency. The first result of a tricuspid insufficiency (see Fig. 180) is a dilatation of the right auricle, because the regurgitating blood distends this chamber during its diastole (p. 382, Law 2). The dilated auricle, having more blood to propel, necessarily hypertrophies (Law 2). It

must then force an increased mass of blood into the right ventricle; the latter chamber, therefore, dilates and hypertrophies (Law 2), and the lesion is compensated in so far as it is possible. The right ventricle, in virtue of its dilatation and in spite of the blood leaking through the tricuspid orifice, is then able to propel sufficient blood with each systole into the pulmonary circulation. Practically, this compensation has very narrow limits, because the systole of the dilated and hypertrophied right auricle does not supply the right ventricle exclusively, but also drives the blood back again into the veins,[1] and, besides, owing to its inherent muscular weakness, the right auricle has not the ability to hypertrophy beyond a certain degree. If in progressively increasing tricuspid insufficiency these limits be reached, the influx of venous blood into the right heart will depend upon the venous pressure, upon the elastic tension of the right auricle's walls, upon the aspiration power

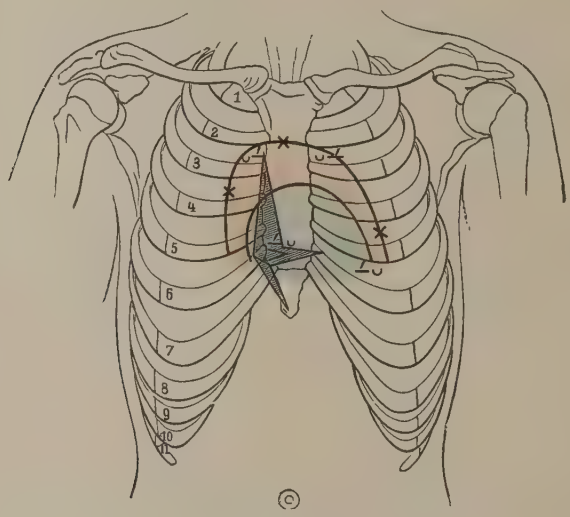


Fig. 181.—Diagnostic diagram of tricuspid insufficiency. (For explanation of the signs see Fig. 172 and p. 388.)

of the thorax, and upon the diastolic suction power of the heart. (See p. 325, foot-note.) The study of the venous pulse in conditions of stasis has made this more evident by showing that too pronounced stretching paralyzes the auricle. (See p. 196. Concerning the causes of such a paralysis see p. 383 et seq.) Under such difficult conditions increasing insufficiency of the tricuspid valve will soon produce the signs of severe stasis, and accompanied by an increasing distention of the venous system, the circulation will ordinarily stop. The prognosis of tricuspid insufficiency is, therefore, much more serious than that of mitral insuffi-

[1] The ring-shaped narrowing of the openings of the great veins in the right auricle which normally during the contraction of the latter (at least according to the statements of physiologists) prevents the reflux of the blood from the right auricle into the veins, must fail in tricuspid insufficiency on account of the dilatation of the right auricle.

ciency unless the former be a relative one, and, with the aid of cardiac tonics, capable of retrogression.

In this lesion a dilatation of the right auricle and right ventricle can be made out by percussion and sometimes by palpation. (See Figs. 181 and 142.) Auscultation discloses a systolic murmur over the tricuspid area (p. 333). This murmur can be differentiated from the murmurs of pulmonary and aortic stenosis by a slight difference in phase (p. 337). During compensation the second pulmonic may retain its normal strength; during disturbance of compensation it may be diminished. The heart tones over the right ventricle may remain normal if the insufficiency be slight, or be weakened if the insufficiency be marked, just as in mitral insufficiency. (See p. 318.) Much the most important and suggestive symptom of tricuspid insufficiency is the coincident ventricular systolic venous pulse (p. 196 et seq.) visible in the jugular veins, often visible as a liver pulse, and visible sometimes even in the small cutaneous veins of the body. The positive venous pulse in the jugular veins is, under some circumstances, accompanied by a systolic tone over the vein, depending upon the systolic tension of the vein-wall and of the valve at the bulb (p. 349). The venous pulse is present both during effective compensation and during disturbed compensation. The ventricular systolic pulse may originate in the absence of tricuspid insufficiency from a paralysis of the right auricle. Concerning a palpable pulsation of the right auricle in tricuspid insufficiency see p. 367. The arterial pulse remains normal during perfect compensation; but such compensation is possible only with slight degrees of tricuspid insufficiency. During disturbed compensation it very quickly assumes a dangerous diminution of volume and tension.

TRICUSPID STENOSIS

This valvular lesion, fortunately, is very rare, both in the congenital and the acquired forms (Figs. 182 and 183). Like tricuspid insuffi-

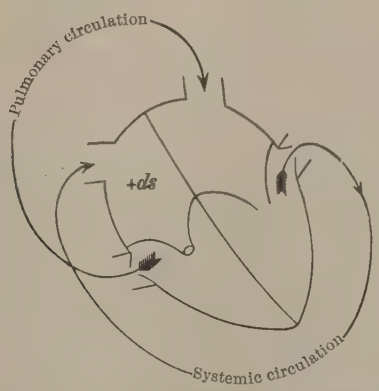


Fig. 182.—Hydraulic diagram of tricuspid stenosis. (For explanation see Fig. 172.)

ciency, it can be compensated with difficulty, and then generally for a short time only. (See Fig. 182.) Compensation takes place in this way: The right auricle, in consequence of the obstruction to the entrance

of the blood into the right ventricle, becomes dilated during the first period of the ventricular diastole, when the auricle is relaxed (p. 382, Law 2). To accomplish the difficult task of emptying its increased contents through the narrow tricuspid opening by its systole it must hypertrophy (Laws 1 and 2). Should this hypertrophy permanently succeed in emptying the auricle completely, the lesion is compensated. But, just as with tricuspid insufficiency, the hypertrophy of so weak a muscular chamber as the right auricle has very narrow limits. Besides, the increased contraction only partially helps the ventricle, because some of the blood is regurgitated into the veins, as in tricuspid insufficiency (see p. 402); moreover, the right auricle is readily paralyzed by decided stretching. (See p. 196 and p. 383 et seq.) Mild degrees of stenosis may, therefore, attain an approximate compensation,

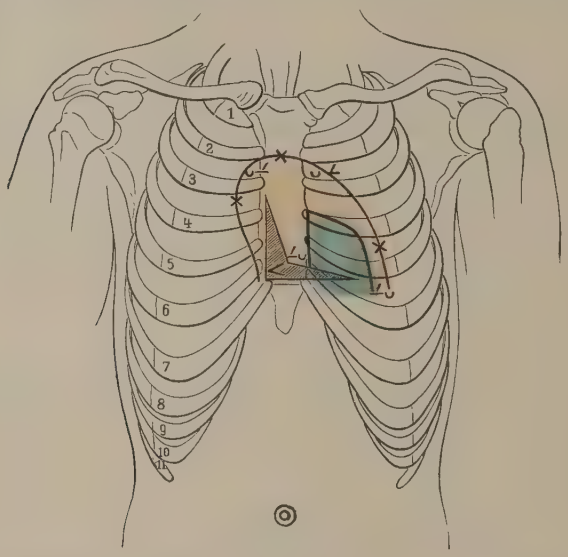


Fig. 183.—Diagnostic diagram of tricuspid stenosis. (For explanation of the signs see p. 388.)

but usually the compensation rapidly disappears. There is this essential difference between mitral and tricuspid stenosis: the latter must be compensated by the aid of the auricle alone, whereas the former has the additional help of the right ventricle. In tricuspid stenosis no reason exists for a dilatation or a hypertrophy of any other heart chamber except the right auricle. The dilatation of the right ventricle, which is sometimes found, probably always depends upon a coincident insufficiency of the tricuspid.

The physical signs (Fig. 183) are a dilatation of the right auricle, demonstrable by percussion or palpation, and a diastolic, a presystolic accentuated, or a pure presystolic murmur, audible over the tricuspid area (p. 335 et seq.). If compensation be well maintained, the second pulmonic tone may be of normal intensity; with disturbance of compensation it becomes very faint. The tricuspid tones, like

the other tones, may retain their normal character during compensation. Concerning the occurrence of an apparent or real accentuation of the first tone at the tricuspid valve in tricuspid stenosis, analogous to the accentuation of the first tone in mitral stenosis, see p. 318 et seq. It is readily understood that the auricular venous pulse is especially marked in tricuspid stenosis. The presence of a (presystolic) auricular liver pulse is credited with diagnostic importance by Mackenzie, but he is contradicted by Volhard.

Under some circumstances a presystolic or diastolic tricuspid tone, analogous to the presystolic or diastolic mitral tone, may be of some diagnostic service (p. 323 et seq.).

PULMONARY INSUFFICIENCY[1]

Pulmonary insufficiency, an inability of the pulmonary semilunar valves to close perfectly, is a rare valvular lesion and usually congenital (Figs. 185 and 186). Its effect upon the lesser circulation is

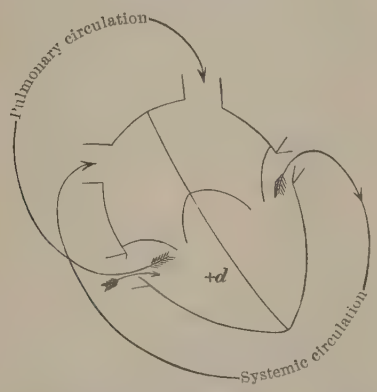


Fig. 184.—Hydraulic diagram of pulmonary insufficiency. (For explanation see Fig. 172.)

analogous to the effect of an aortic insufficiency upon the greater. Compensation (see Fig. 184) will be understood by referring to that lesion. In this lesion it depends upon dilatation and hypertrophy of the right ventricle.

The diagnostic signs consist essentially in a diastolic murmur heard over the pulmonic area (Fig. 185), and transmitted downward (p. 333), and in the demonstrable dilatation of the right ventricle. The diastolic murmur, unlike that of aortic insufficiency, is not transmitted to the neck vessels. The tones are generally normal, just as in aortic insufficiency. The *pulsus celer* belongs to the pulmonary circulation, and, so, naturally escapes notice, or at most betrays itself only by an exceptional pulsation of the pulmonary area, provided the latter be not covered by lung tissue (analogous to the increased aortic pulsation in aortic insufficiency, p. 396 et seq.). The lack of a *pulsus celer* in the peripheral arteries aids in distinguishing pulmonary from aortic insufficiency.

[1] See Gerhardt, Ueber Schlussunfähigkeit der Lungenarterienklappen, Verhandl. des II. Cong. f. inn. Med., 1892, p. 290.

Gerhardt[1] has called attention to the occurrence of a double tone audible over the lung at some distance from the heart, *i. e.*, outside of the right scapula (analogous to the double femoral tone of aortic insufficiency, p. 348); also of a cog-wheel or jerky respiratory murmur synchronous with the pulse and heard at some distance from the heart. He attributes the latter phenomenon to the vigorous systolic distention of the lung vessels by the pulmonary *pulsus celer*. Both signs are, to a certain extent, the audible evidences of a *pulsus celer* of the pulmonary

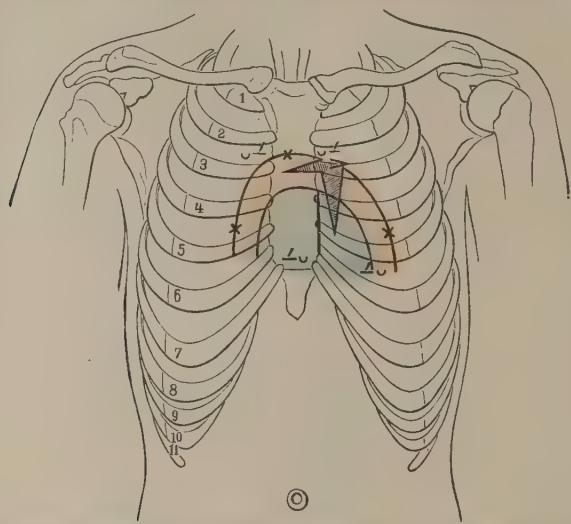


Fig. 185.—Diagnostic diagram of pulmonary insufficiency. (For an explanation of the signs see p. 388.)

artery. Concerning this, see the explanation of jerky respiratory murmurs synchronous with the pulse, especially upon p. 288 et seq.

Von Pawinski[2] has called attention to the appearance of a relative insufficiency of the pulmonary artery in mitral stenosis from the mechanical dilatation of this artery.

PULMONARY STENOSIS

Pulmonary stenosis (Figs. 186 and 187) is the most frequent of all congenital valvular lesions, and, therefore, has considerable practical importance. Hypertrophy of the right ventricle (see Fig. 186) is essential for its compensation (Law 1), and develops according to the principles mentioned under Aortic Stenosis. To this hypertrophy dilatation is added secondarily by disturbances in the compensation, or sometimes without them (Law 4).

The essential physical sign is the systolic murmur audible over the pulmonic area and the right ventricle, and often over the entire lung, corresponding to the branches of the pulmonary artery. In distinction to the systolic aortic murmur, the murmur of pulmonary stenosis is not transmitted into the vessels of the neck. Sometimes it may be differentiated from the systolic auriculoventricular murmur by a slight difference in phase (p. 336). There is generally nothing characteristic about the tones. There may be no demonstrable dilatation of the right

[1] Loc. cit.

[2] Deut. Arch. f. klin. Med., 1894, vol. lii.

ventricle, because in a typical case this chamber at first simply hypertrophies. But ordinarily a paralytic dilatation (Law 4) soon occurs,

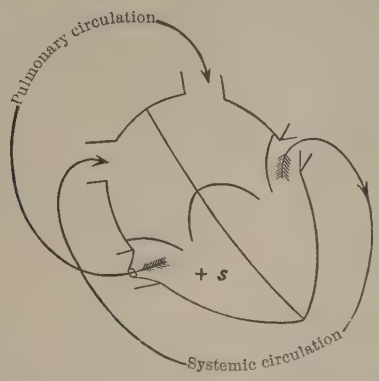


Fig. 186.—Hydraulic diagram of pulmonary stenosis. (For explanation see Fig. 172.)

becomes anatomically fixed, and the heart is then plainly enlarged to the right.

Pulmonary stenosis is almost exclusively congenital, and is frequently combined with pulmonary phthisis and clubbed fingers (p. 64). Con-

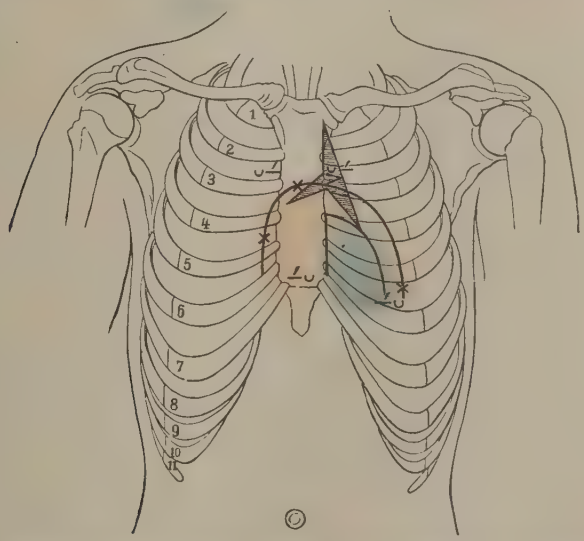


Fig. 187.—Diagnostic diagram of pulmonary stenosis. (For an explanation of the signs see p. 388.)

cerning the well-marked cyanosis usually resulting from this lesion, as well as the combination with other anomalies of the heart, see the section on the Congenital Valvular Lesions.

DIAGNOSIS OF COMBINED VALVULAR LESIONS

The diagnosis of single valvular lesions generally seems comparatively simple; but it is sometimes no easy task to distinguish correctly several lesions, when, as so frequently happens, they are present together. The relations become complicated, because one valvular lesion influences the other in regard to the changes of pressure within the heart. This influence may be expressed by the relative intensity of the heart tones, by the presence of dilatation and hypertrophy of individual chambers, and by the peculiarity of the pulse. With combined valvular lesions the clinician's task assumes a special difficulty, because he must analyze complex murmurs into several individual ones, determining their origins, and decide which are systolic and which are diastolic.

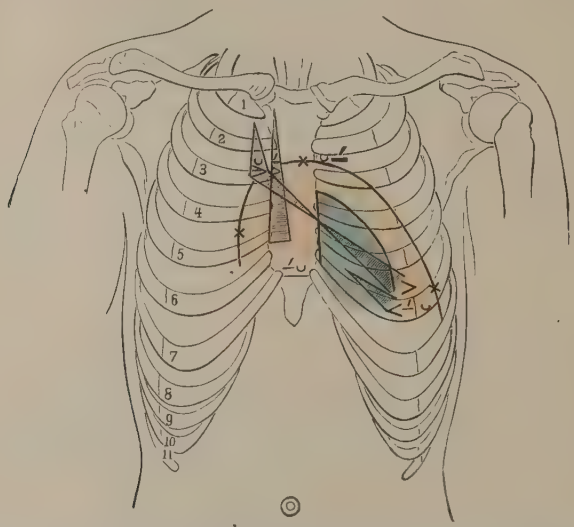


Fig. 188.—Diagnostic diagram of a complicated valvular lesion: Mitral insufficiency and stenosis and aortic insufficiency, possibly an aortic stenosis as well. The last cannot be diagnosed from the cardiac signs alone. The pulse must first be carefully examined. (For an explanation of the signs see pp. 338 and 388.)

The most important rule for the diagnosis of such complicated cases is to heed only those physical signs which are characteristic of a single valvular lesion; then, starting with the supposition that this lesion is actually present, to analyze the other signs and determine whether any sign disproves this supposition, and, further, to decide whether all the signs can be explained on this one hypothesis. If one lesion be insufficient to explain all the signs, those not yet explained should be considered further. In this way, step by step, we can complete the diagnosis of combined valvular lesions. The task may be lightened by first considering the more frequent valvular lesions; and, in case there is no question of a congenital disease, in neglecting the more unusual lesions of the right heart, unless, of course, some signs remain which cannot be explained by the supposition of only left-sided

changes. For illustration: suppose, in a case with several murmurs, a plain presystolic murmur can be heard at the apex. This murmur is in all probability due to a mitral stenosis, because tricuspid stenosis is so rare. We then try to see if this hypothesis will explain all the signs. If a systolic murmur can also be heard, we must search for some other cause. We estimate its maximum point, its relations of transmission, its exact phase (p. 334 et seq.), and under some circumstances the peculiarity of the pulse (aortic stenosis), and soon decide whether this systolic murmur arises at the aortic or at the mitral orifice. We then diagnose two lesions—a mitral stenosis and insufficiency—and review the clinical picture to determine whether all the signs are satisfied, or whether, perhaps, we need to assume a third lesion. And so, step by step, we arrive at a complete diagnosis.

To distinguish whether a murmur audible over a large area of the heart arises at one or more places—in other words, whether it be composed of several different murmurs—we should construct a figure of the minimum points, according to the rules on p. 337 et seq. This method is very important in diagnosing combined valvular lesions.

A careful attention to the evidences in the vessels (peculiarity of the pulse, degree of the cyanosis, venous pulse, arterial tones, etc.) will give just as important information for the diagnosis of combined as of single lesions.

In general, here as well as everywhere else, the systematic analysis of a clinical picture can be acquired only by considerable practice, and even then only after thorough reflection.

Fig. 188 illustrates such a combined valvular lesion.

CONGENITAL VALVULAR LESIONS; ABNORMAL COMMUNICATION OF THE HEART CAVITIES; ADMIXTURE CYANOSIS

Experience has taught us that in making diagnoses of acquired valvular lesions we can narrow the probabilities to those of the left heart, excepting the possibility of the rather rare tricuspid insufficiency. [Relative tricuspid insufficiency is a commoner lesion than is usually believed.—Ed.] In congenital lesions we can confine our attention mostly to the right heart, because it is this side which is most frequently affected during intra-uterine life. Perhaps the reason is that during this period the right ventricle is under relatively higher pressure than during extra-uterine life, since it supplies blood not only to the pulmonary circulation by means of the pulmonary artery, but also to part of the systemic circulation by means of the ductus Botalli (ductus arteriosus). Hence the right heart is more exposed to injuries in which this mechanical factor plays a part (infection and endocarditis), just as the left heart is in adults. Besides embryonic arrests of development and malformations also contribute decidedly to the right-sided location of congenital heart affections. It is well to note that such malformations may result from right-sided intra-uterine congenital valvular lesions of endocardial origin, because of the creation of abnormal relations of pressure or current. Naturally, then, the right heart would be most frequently involved by such secondary malformations.

The great difficulty in the diagnosis of congenital heart disease is that, besides the valvular lesions which depend upon endocarditis, there are very often developed obstructions, malformations, abnormal communications between heart cavities, etc., and all these are mutually influenced, etiologically and symptomatically, in a very complicated way.

The most frequent and practically important malformations and obstructions to be considered in the diagnosis of congenital lesions are: a *patent foramen ovale, ventricular septum, or ductus Botalli; origin of the aorta from both ventricles; connection of the pulmonary artery, closed at its origin, with the aorta through the ductus Botalli* (the right heart must then communicate with the left through the foramen ovale, or through an opening in the ventricular septum); *transposition of the great vessels*, so that the aorta comes from the right, the pulmonary artery from the

left, ventricle; *obliteration of the aorta at the entrance of the ductus Botalli* (in this case life is preserved by the formation of a collateral circulation between the upper and the lower part of the aorta). It need not be said how difficult it is to recognize these conditions, whether they appear isolated or as complications of fetal valvular defects. Only a few hints can be given in the present state of diagnosis.

Much stress is ordinarily laid upon the exceptionally pronounced cyanosis which appears so frequently in congenital heart disease, and which we are inclined to attribute to the admixture of venous with arterial blood through some communication. The conditions are, however, especially favorable for a high grade of cyanosis in right-sided valvular lesions, without supposing the admixture of arterial and venous blood, because, on the one hand, compensation is here either very poor or soon disturbed (*e. g.*, tricuspid lesions), and because, on the other hand, in all right-sided, even in pulmonic, lesions, as soon as there is a disturbance in compensation, the stasis must be concentrated in a most direct and intense way upon the systemic veins, whereas in left-sided valvular lesions the lung serves as a large reservoir for the stagnating blood. Therefore, in congenital cardiac disease it is incorrect to make a diagnosis of an abnormal communication and consequent admixture of arterial and venous blood simply from marked cyanosis. Many authors even go so far as to deny the possibility of such admixture cyanosis, on account of certain mechanical considerations. They are supported with some reason by the fact that communications between the ventricles and between the auricles have sometimes been found at autopsies without any signs during life of such a cyanosis. And they contend that this lack of admixture cyanosis (despite the communication) is not surprising, because the two abnormally communicating heart cavities contract coincidentally, so that no blood need be sent from one to the other. Certainly, every abnormal communication of the cardiac cavities does not cause admixture cyanosis, but it is probable that under certain conditions venous blood may be mixed with arterial. The following examples may be cited in evidence:

A mere defect in the septum between the auricles or the ventricles ordinarily causes no admixture cyanosis; yet it is perfectly easy to understand that such an effect may result if, at the same time, a right-sided valvular lesion be present also. With tricuspid insufficiency, for example, and an open foramen ovale, the ventricular systole may force the venous blood out of the right ventricle not only into the right, but also, in consequence of its increased pressure, into the left, auricle. With tricuspid stenosis, during ventricular diastole, the blood from the right auricle may partly flow in the direction of least resistance through the foramen ovale into the left auricle and ventricle. Just so it is conceivable that in pulmonary stenosis during systole the blood from the right ventricle is forced into the left ventricle through a patent ventricular septum, the presumption being that the right ventricle has become so strongly hypertrophied that it overbalances the aortic pressure which acts upon the other side of the communicating orifice.

The plainest and, perhaps, also most frequent example of admixture cyanosis is "straddling" of the aorta, *i. e.*, its origin from both ventricles and insertion above the defect in the ventricular septum. Here, of course, the aorta must contain mixed blood. We observe this appearance in congenital pulmonary stenosis.

Patency of the ductus Botalli, on the contrary, is alone hardly sufficient to cause admixture cyanosis, because the aortic pressure, if no other anomaly be present, is always higher than that of the pulmonary artery, so that the blood could pass through the aorta into the pulmonary artery, but not in the reverse direction. But mixed blood must flow into the aorta if the ductus Botalli is the only outlet of the pulmonary artery, which is completely closed at its opening into the right ventricle, because the aorta must obtain its blood from the opening in the ventricular septum, *i. e.*, from the right ventricle.

In congenital valvular lesions, therefore, it is reasonable to assume the possibility of admixture cyanosis, and to be fairly certain of its presence, if the cyanosis be very pronounced while the veins are very little dilated (marked cyanosis with slight stasis).

In any given case, however, the cause of the admixture cyanosis is not so easily determined. In tricuspid lesions we should naturally first suppose an open foramen ovale; whereas in pulmonary stenosis a patent ventricular septum, with or without a straddling aorta, would be more probable. Under some circumstances a systolic murmur at the cardiac apex may be a positive sign of a ventricular septum defect. This sign is, however, of very little practical value, because in pulmonary stenosis just where a patent ventricular septum is to be taken into consideration the systolic murmur is frequently very plainly audible over the entire heart, since it proceeds from the entire right ventricle (p. 333, 7.)

It is difficult to diagnosticate patency of the ductus Botalli. We should remember that this anomaly very often accompanies congenital pulmonary stenosis. Zinn and Hermann Müller[1] have called attention to a band-like dulness reaching upward and to the left of the upper part of the sternum. They attribute this to the dilatation of the overburdened pulmonary arteries which results from the aortic pressure. An accentuation of the second pulmonic has been repeatedly stated to be a result of a patent ductus Botalli, because with this abnormality the pulmonary arteries are affected by the aortic pressure. Müller attributes diagnostic significance to the systolic and diastolic murmurs which appear over the great vessels, and states that they sometimes merge into a practically continuous murmur. The systolic murmur depends upon the systolic passage of blood from the aorta through the narrow ductus Botalli into the pulmonary aorta; the diastolic murmur, upon the diastolic continuation of this current. The congenital obliteration of the aorta at the place of origin of the ductus Botalli is, on the contrary, very easy to diagnose, whether it be associated with congenital valvular lesions or isolated. The collateral circulation, by which the blood flows from the peripheral arteries of the upper part of the body (subclavian, etc.) to the lower part of the aorta, becomes visible under the skin and makes the diagnosis clear. Such an obliteration may exist without any disturbances of the circulation.

There are many questions in the pathology and diagnosis of congenital heart lesions which still lack solution.

THE DIAGNOSIS OF DEFECTS OF THE VENTRICULAR SEPTUM

The work of H. Roger,[2] and more especially that of H. Müller,[3] upon the clinical and postmortem findings in cases of defects of the ventricular septum show that it is possible to diagnose this lesion from its clinical picture. One of the most important elements of their work was to demonstrate that defects of the ventricular septum occur alone and uncomplicated much more frequently than has been supposed, and thus correspond to a clear and simple clinical picture. Litten[4] was responsible for the current belief that these defects are usually accompanied by other anomalies, such as defects of the auricular septum, pulmonary stenosis, patent ductus arteriosus, etc. Such a belief thoroughly discouraged attempts to diagnose the condition and made the interpretation of the systolic murmur accompanying a defect of the ventricular septum very difficult. In France, Roger's work long ago led to the acceptance of a clinical picture of this anomaly, and there the disease is known as *la maladie de Roger*. Müller's work, with the abundant material presented by him, deserves the credit for calling attention of the German profession to the condition under discussion. Roger states the characteristics of the disease in the following words, quoted almost verbally in Müller's paper.

1. Defective ventricular septum is a congenital anomaly of the heart which is quite compatible with longevity; it sometimes occurs without an accompanying pulmonary stenosis, does not in itself lead to cyanosis, and it can be diagnosed during the patient's life.

2. The diagnosis is based chiefly upon the auscultatory findings. The characteristic sign is a loud, prolonged, rushing or purring murmur (*bruissement*), which is quite unique in character. This murmur begins during systole and continues in such a manner as to obscure completely the normal "tic tac" of the heart; it is most intense not at the apex, as in mitral disease, nor at the base to the right of the sternum, as in aortic stenosis, nor to the left of the sternum, as in pulmonary stenosis, but in the upper third of the precordia; it is heard best in the median line corresponding to the median position of the septum itself, and gradually diminishes in intensity toward the lateral regions of the precordia; it is sharply localized, is not transmitted into the vessels, and is frequently accompanied by a well-marked thrill. A murmur with the above characteristics forms, according to Roger, a pathognomonic sign of a defect of the ventricular septum. This writer does not mention the size of the heart or the character of the heart sounds. Müller likewise strongly emphasizes the auscultatory phenomena for the diagnosis of the condition, and lays stress upon the loudness of the murmur, which quality he ascribes

[1] Correspondenzbl. f. Schweizer Aerzte, 1889, p. 449.

[2] Bull. de l'acad. de med., 1879, No. 42, translated by Löffler in Med.-Chir. Centralblatt, Vienna, 1881, xvi, and Revue de méd., Paris, 1879, p. 681.

[3] H. Müller, Zur Lehre von den angeborenen Herzkrankheiten, Correspondenzbl. f. Schweizer Aerzte, 1904.

[4] Deut. med. Woch., 1887, p. 144.

to its production by a stream of fluid under pressure, sent through the narrow septal opening during systole. Frequently the murmur is very rough and so loud that it is hardly exceeded in intensity by the sounds heard in mitral insufficiency or in pulmonary stenosis, thus approaching most in character the murmur of aortic stenosis. Occasionally it may be heard a few centimeters away from the chest-wall, though it does not possess any real musical tone. Müller adds that the well-known device of moving the ear a slight distance from the stethoscope enables one to hear a systolic tone accompanying the murmur. As has been noted, the murmur is not, properly speaking, transmitted into the vessels, but it is loud enough to be audible in the neck as well as behind, especially in the left interscapular space. Müller noted that the second pulmonic tone was generally neither accentuated nor weakened; in two cases only was it accentuated, in one of which there was a dilatation of the pulmonary artery. In none of Müller's cases was a murmur audible during the diastole, the reason being that the cusps of the mitral and the tricuspid valves shut off the defect in the ventricular septum in this period; and that during diastole the difference of pressure in the two ventricles is not sufficiently marked to result in the passage of any considerable stream of blood from one chamber to the other. Keim alone describes a diastolic murmur in addition to the systolic, but Müller suspects that in this case an open ductus arteriosus complicated the septal lesion. Müller lays special stress upon the site of the murmur, the point of maximum intensity being found beneath the third rib at the left sternal margin, that is, at the spot where the projection of the defect in the septal wall, which is always found in its upper part, would intersect the surface of the chest. In two cases the murmur was likewise very distinctly heard in the second left interspace, thus favoring the possibility of mistaking pulmonary stenosis for the lesion. At the mitral area and toward the apex of the heart the murmur was usually less intense. It is also audible, though much fainter, at the right of the sternum. As Roger has already emphasized, this murmur is never most intense at the site of auscultation of the mitral, aortic, or pulmonic area. A well-marked thrill was present almost constantly at the point of maximum intensity of the murmur; occasionally a thrill was to be felt over the sternum and at the right sternal margin; and in one case (with dilatation of the pulmonary artery) a thrill could be appreciated over that artery. In contrast to Roger, Müller describes very carefully the changes in the size of the heart which may be produced by the defects of the ventricular septum. In early life there may be no increase in the size of the heart; later the right ventricle and the left ventricle also may become hypertrophied and dilated. In the author's opinion these changes in the size of the heart are easily explained by the laws of compensation. (See p. 382.) In cases in which the heart is not found to be hypertrophied it may be supposed that the character of the defect is such as to result in a murmur, but not to produce any hydrodynamic effects upon the blood current.

The changes in size may be explained as follows: The two ventricles are compelled to work to a certain degree against each other, much as in mitral insufficiency. The high pressure in the left ventricle compels the right chamber to exert more force, and thus it hypertrophies. Because of the increased work, it may likewise become dilated, especially as it receives an extra amount of blood from the left ventricle. (Compare the circumstances in mitral insufficiency, see p. 388 et seq.) Indeed, everything said about the conduct of the right ventricle in mitral insufficiency applies in this connection, and the analogy extends still further to the behavior of the left ventricle. If the right ventricle become not only hypertrophied, but also dilated, which occurs in marked defects of the septum, it delivers increased amounts of blood to the left heart by way of the pulmonary circulation. In consequence the left side likewise dilates, the left auricle as well as the ventricle sharing in the changes produced, as in mitral insufficiency, the active factor being the oscillation of the blood forward and back through the mitral opening. Again, just as in mitral insufficiency, the left heart is overfilled during diastole, and, compelled to do an increased amount of work, becomes hypertrophied.

This presentation of the compensation of the circulation forces the author, at least, to conclude that the differential diagnosis between the septal lesion discussed and mitral insufficiency, especially when one is not aware of the congenital character of the lesion, is not without difficulty; indeed, he has had practical evidence of the truth of this conclusion. The difficulty depends especially upon the fact that in mitral insufficiency, as we have seen (p. 333), the murmur may best be heard at the site of maximum intensity of the murmur of a congenital defect of the septum if the surface of the heart be abnormally exposed; moreover, the second pulmonic sound may not be accentuated in mitral insufficiency, and, on the other hand, as we have just learned, it may be accentuated when there is a defect of the ventricular septum.

Indeed, Müller observed two cases with such an accentuation. A dilatation of the pulmonary artery in certain cases furnishes further difficulties in diagnosis, for then mistaking the lesion for an open ductus arteriosus is quite possible, as an experience of Müller's very well shows. The presence of a characteristic dulness to the left of the sternum, caused by the dilated artery, led Müller to diagnose a patent ductus arteriosus; the autopsy, however, showed that the lesion consisted of a defect of the ventricular septum, accompanied only by a dilatation of the pulmonary artery. The cause of such dilatation of the pulmonary artery is to be sought in all probability in the increased energy of the right ventricle. The point of differentiation between an open ventricular septum and a patent ductus arteriosus may be considered to consist in the presence of a systolic and a diastolic murmur in the latter case. (See p. 412.) However, in spite of these undisputed difficulties, the diagnosis of defects of the ventricular septum seems often to be quite easy, and especially is this the case when no changes have taken place in the size of the heart. The latter point is valuable because absence of increase in the size of the heart is probably never to be noted in any other condition accompanied by such well-marked murmurs. In addition, the very intensity of the murmurs is of diagnostic significance. Finally, both Roger and Müller have remarked the absence of cyanosis in these cases, except when they are accompanied by marked pulmonary changes, such as catarrhal pneumonia, observed twice, and miliary tuberculosis, observed once.

ANEURYSM OF THE AORTA

Aortic aneurysms are most frequently situated upon the ascending aorta or upon the arch of the aorta. When an aneurysm reaches a certain size, we can detect a prominence in the upper intercostal spaces to the right of the sternum, and appreciate it by palpation as well. Small aneurysms may not exhibit any prominence; and

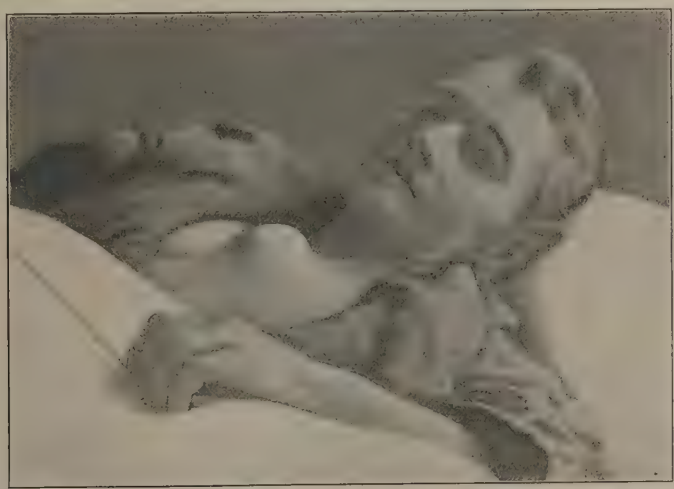


Fig. 189.—Large aneurysm of ascending and transverse arch of aorta (New York City Hospital).

the pulsation can only be appreciated by palpation. Valuable information may also be afforded by palpation with the stethoscope. (See Auscultatory Palpation, p. 356.) If the aneurysm reach to the surface, percussion will show a marked dulness generally continuous with the cardiac dulness, and, being a superficial dulness, is most plainly brought out by very light percussion. If a layer of lung remain in front of the aneurysm, the dulness may be either entirely absent or there may be only a moderate, deep dulness, demonstrable by strong percussion. Even here, the pulsation may be transmitted through the overlying layer of lung to the surface. Auscultation very frequently reveals a systolic murmur, which may sometimes be appreciated by palpation. The entrance of the blood into the aneurysmal sac produces

this murmur as a result of a change of lumen in the blood-path. (See Fig. 103, III, and p. 328 et seq.) This murmur, like that of aortic stenosis, is transmitted most distinctly in the direction of the aortic current, *i. e.*, to the neck vessels. Diastolic murmurs are, however, sometimes due to aneurysms. The proof that such a murmur arises from the regurgitation of blood into the sac, which is stretched during diastole and not from a complicating aortic insufficiency, is furnished by the existence of similar murmurs over aneurysms of the abdominal aorta.[1] Under some circumstances a diastolic murmur may be one of the earliest signs of an aortic aneurysm, and may readily lead to a confusion with aortic insufficiency unless the aneurysm is evident to inspection, palpation, and percussion. Frequently, however, the diastolic murmur over an aortic aneurysm depends upon the coexistence of an aortic insufficiency. For the sac, continually increasing in size, gradually produces a dilatation of the aortic orifice, and so a relative insufficiency, or else the endarteritis, which is always present in an aneurysmal aorta, attacks the valves as well. Unless an aortic aneurysm be combined with a valvular lesion, the heart need not be hypertrophied nor dilated, because an aneurysmal dilatation of the aorta by

Fig. 190.—Aneurysm of the descending arch of the aorta (Dr. Cutler, Massachusetts General Hospital).

itself offers no considerable obstacle to the circulation. Large aneurysms, on the contrary, generally crowd the heart somewhat to the left, so that the apex-beat lies further outside than normally. To determine the exact seat of the aneurysm in relation to the origin of the innominate and of the left carotid and left subclavian arteries, we should accurately compare the exact time and strength of the carotid and radial pulses on the two sides, both by palpating and by the use of the sphygmograph. The aneurysmal dilatation frequently delays the pulse in those arteries which arise from the aorta beyond the aneurysm, because a sort of air-vessel action retards the pulse-wave. In other cases the delay is due to the fact that some of the arteries arise from the sac itself and are narrowed at their origin. The pulse in such an artery may then be also abnormally small and delayed by crest-retardation. (See p. 151 et seq.) In many cases certain accompanying signs which are to be attributed to the pressure of the aneurysm are important in confirming the diagnosis: pressure upon the trachea, with dyspnea; upon the esophagus, with difficulty in swallowing; upon one of the bronchi (generally the left), with a diminished respiratory

[1] Von Leyden, Deut. med. Woch, 1900, No. 23, p. 365 et seq.

murmur over the corresponding lung; upon the left, rarely upon the right, recurrent laryngeal, with a unilateral vocal paralysis, involvement of the sympathetic with unequal pupils. A venous collateral circulation, visible in the skin over the chest, is of the same diagnostic importance for an aneurysm as for other intrathoracic tumors (p. 60 et seq.). It results from the pressure of the aneurysm upon the great veins inside the thorax. Mention should be made of the *Oliver-Cardarelli sign* (tracheal tug) (p. 366). The symptoms of the rare aortic aneurysms which are situated at some distance from the great vessels of the heart (thoracic and abdominal aorta) can be readily deduced.

In consequence of the increased systole of the left ventricle, an aortic insufficiency may cause a considerable diffuse dilatation of the ascending aorta and produce a striking pulsation and dulness over the upper intercostal spaces to the right of the heart. (See Fig. 143.) Severe pain is also a symptom in this condition, so there may be some difficulty in the differential diagnosis between it and a true saccular aneurysm. The most important criteria pointing to a saccular aneurysm are the exhibition of compression signs (recurrent paralysis, etc.) of the Oliver-Cardarelli phenomenon (see p. 366), and of difference in the pulses and pupils. If an aneurysm form a circumscribed, prominent tumor, dull to percussion, there will be no possibility of confusion.

Recently the Röntgen rays have been repeatedly employed in the diagnosis of aortic aneurysm. They allow of certain conclusions, however, only when the aneurysm is in the form of a pulsating tumor which is distinctly separated from the heart. These are cases in which other methods of examination usually determine the diagnosis. In contrast to these cases, there are many others in which the Röntgen examination will not certainly differentiate an aortic aneurysm from a diffuse dilatation of the aorta due to aortic regurgitation, or even from a dilated right ventricle. For the details of the Röntgen examination the reader is referred to the special works upon the subject.

PERICARDITIS

Physical examination generally reveals a *dry pericarditis* by a characteristic rubbing friction sound. (See p. 344 et seq.) So long as the

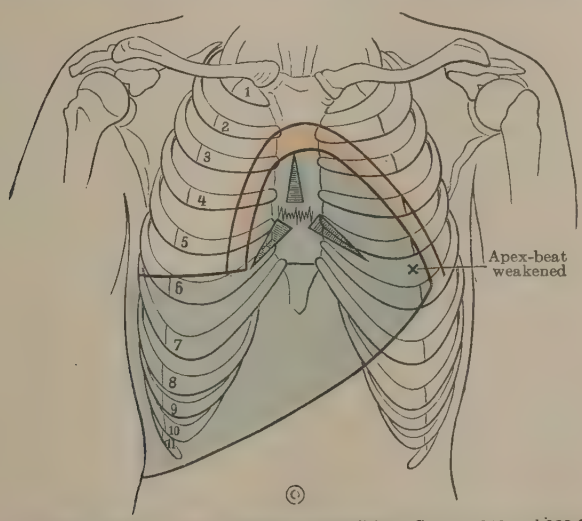


Fig. 191.—Diagnostic diagram of an exudative pericarditis. (See pp. 338 and 388 for an explanation of the signs.)

layers of the pericardium are not separated from one another by a fluid exudate throughout their entire extent, *exudative pericarditis* will also

cause a pericardial friction rub, because there is always a deposition of exuded fibrin in addition to the fluid (p. 345). The cardinal sign of *exudative pericarditis* is, however, a characteristic cardiac dulness which is increased upward; and which ordinarily assumes the form of a triangle with its base below (p. 248 et seq.). The right cardiopulmonary angle is decidedly blunted. The width of this dulness is increased in the sitting or erect posture (p. 248 et seq.). The apex-beat is weakened (p. 360), and the heart tones are also enfeebled (p. 316), especially in the outer portions, on account of the interposed exudate. In some cases the apex-beat lies within the borders of superficial cardiac dulness (p. 360 et seq.), and frequently there is a visible prominence of the precordia (p. 34). Beyond these features the diagram (Fig. 191) will illustrate the entire clinical picture of exudative pericarditis. Such a border of deep cardiac dulness is often lacking (see p. 242 et seq.), and the heart is apparently laid bare by the crowding back of the lungs, causing only a very large superficial dulness. (See p. 361 et seq. in regard to the diagnosis of pericardial synechiæ and cardiomediastinal adhesions. These have recently assumed an importance as indications for cardiolysis.)

GRAPHIC EXPRESSIONS FOR THE PHYSICAL SIGNS IN PULMONARY CASES

In the sections upon Percussion, Auscultation, Inspection, and Palpation of the lungs we have described and explained the occurrence and the significance of the individual physical signs of pulmonary and pleural affections, and so now we need only add a concise abstract of our method of combining these signs in order to make a general picture in any given case. The arrangement of the elementary symptoms in pulmonary and pleural affections is manifold, and so much greater than in cardiac affections, that it is obviously impossible to treat the former as completely as the latter have been dealt with in the preceding pages. The author has, therefore, merely added a few charts. For the sake of simplicity and brevity we employ graphic expressions to describe the lung conditions. These have been found, in the clinic at Bern, both practical and comprehensive.

The rules for such graphic expression are simple and easily memorized. We represent the respiratory murmur audible over a certain area of the lung by a small right angle, and mark it at the corresponding spot upon a chest diagram. This sign may be modified in various ways, according to the modification of quality of the respiratory murmur. The vertical limb of the angle represents the inspiratory murmur; the horizontal, the expiratory murmur; the length of the limb shows its duration; the thickness, its intensity. A simple, smooth, straight line signifies normal vesicular breathing; a dotted line, cog-wheel breathing; a toothed line, rough vesicular breathing. A small cross-line on the limb signifies mixed breathing; two cross-lines, pure

bronchial breathing. From these rules we can readily understand the following:

L Vesicular breathing.

L Weak vesicular breathing (diminished).

L Coarse vesicular breathing.

L Coarse vesicular breathing with prolonged expiration.

L Rough vesicular breathing with prolonged expiration.

Bronchial breathing.

Mixed (bronchovesicular) inspiration with bronchial expiration.

Vesicular inspiration with bronchial expiration.

Mixed (bronchovesicular) inspiration with prolonged expiration.

Cog-wheel vesicular breathing.

Cog-wheel inspiration with bronchial expiration.

Indistinct (feeble) breathing, etc.

The râles are designated thus:

Dry râles:

Sonorous and sibilant.

Crackling (creaking).

Moist râles:

(*a*) Non-consonating or non-resonant.

Large, coarse,
Small, fine,
Medium,
Mixed,
} Moist or bubbling.

(*b*) Consonating or resonant.

Large, coarse,
Small, fine,
Medium,
Mixed,
} Moist or bubbling.

Inspiratory râles are designated by prefixing the letter "i"; expiratory, by prefixing "e"; *e. g.*,

Inspiratory, non-consonating, mixed moist or bubbling râles, "*i*∴."

Inspiratory and expiratory sonorous and sibilant, *ie* ∼.

Crepitant râles (crepitation) are designated by Kn.

A pleuritic or a pericardial rub is designated by the sign: ⩘, ⩘. If it be possible to confuse a pleuritic with a pericardial rub, "pl" or "pe" should be prefixed.

Tone phenomena are expressed as words, or abbreviations may be used, as:

ty = tympanitic note.
hty = high tympanitic note.
lty = low tympanitic note.

In recapitulation we may mention (see p. 217) that a blue surface corresponds to the superficial dulness (*i. e.*, with light percussion).

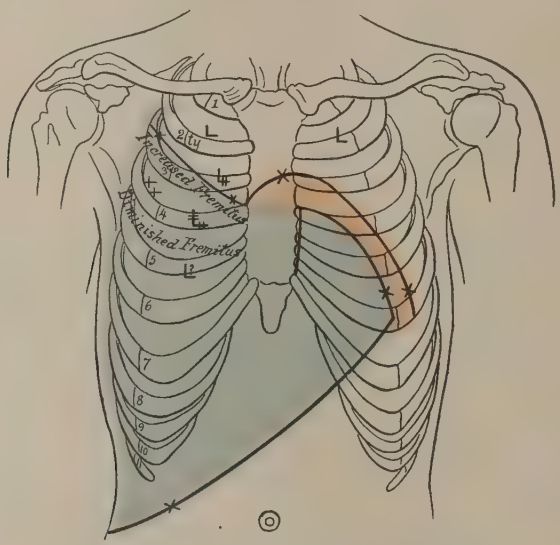


Fig. 192.—Physical signs in right pleurisy with effusions.

the red, to the deep dulness. A mixed color is employed for a dulness which can be demonstrated as well by deep as by superficial percussion. The intensity of the color represents the intensity of the dulness. Palpable borders are represented in black. The border lines are generally so drawn that the form of dulness and the direction of the lines correspond as nearly as possible to the reality.

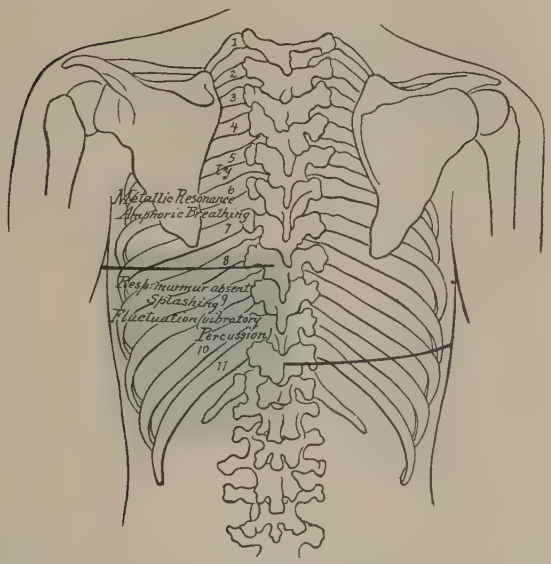


Fig. 193.—Physical examination in left pyopneumothorax. (See Fig. 148.)

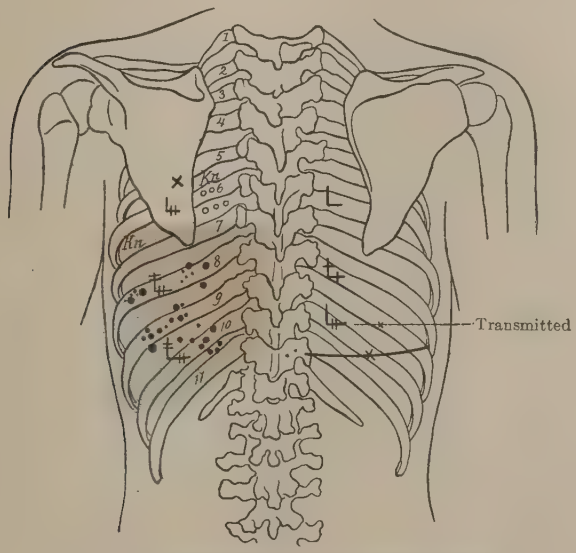


Fig. 194.—Physical examination in left croupous pneumonia.

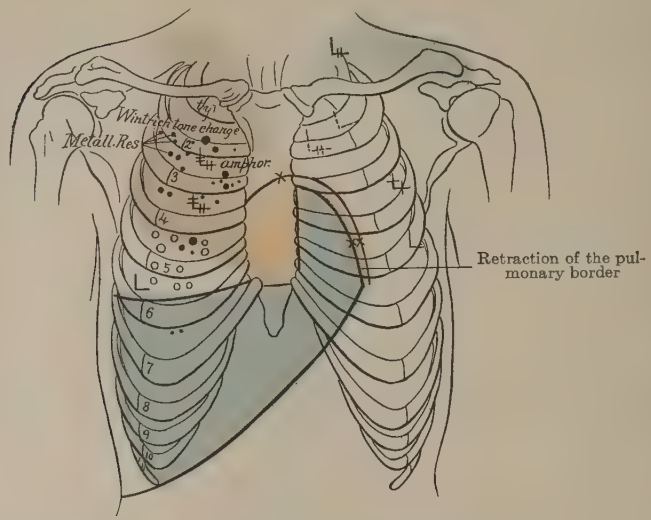


Fig. 195.—Physical signs in pulmonary phthisis: Marked change on the right; beginning on the left.

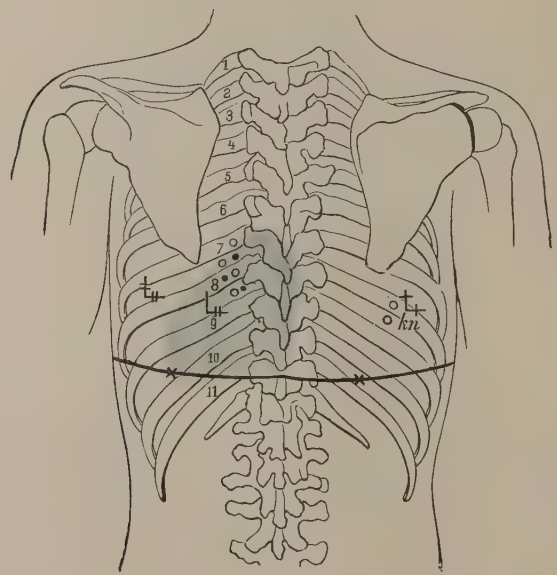


Fig. 196.—Physical signs in catarrhal pneumonias, infarcts, etc.

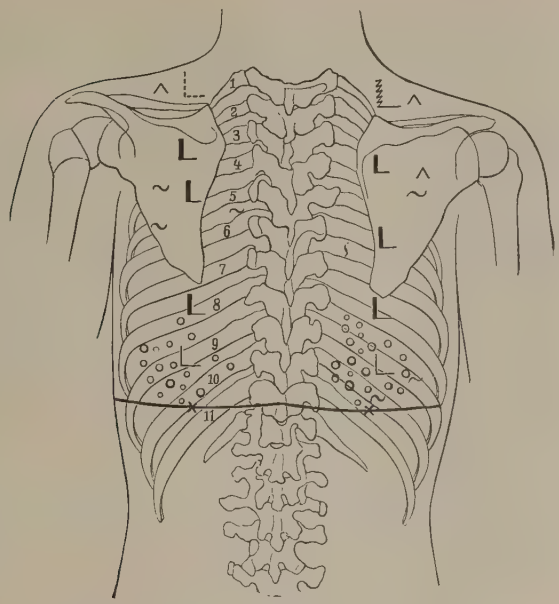


Fig. 197.—Physical examination in diffuse bronchitis.

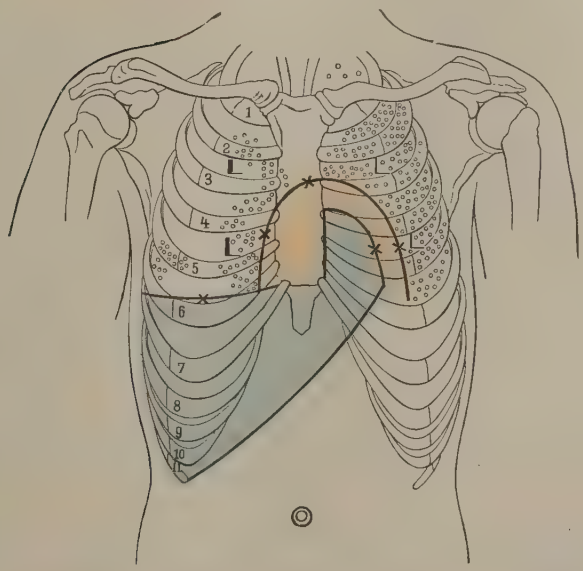


Fig. 198.—Physical examination in capillary bronchitis or miliary tuberculosis.

EXAMINATION OF THE STOMACH AND STOMACH-CONTENTS

Under the examination of the stomach we shall consider not only the estimation of its size and position, and whatever other results may be determined by palpation (tenderness, demonstration of tumors, etc.), but more particularly the methods of testing its specific functions. Purely physical methods of examination furnish such meager results that we must depend upon the last-named methods for most of the diagnostic points. Therefore, the bulk of the following section will be devoted to the functional examination of the stomach, and especially to the study of its secretion relations. Under the examination of air-containing abdominal viscera the author has already alluded to many points in physical diagnosis. (See pp. 257 et seq., 277 et seq., and 368 et seq.) He has intentionally postponed until now any more minute consideration of the physical methods of examining the stomach, because such methods reveal but isolated symptoms which are of no value except in connection with others.

Many of the cases require the employment of the stomach-tube, although its use is attended with certain discomforts, and at times even with injuries, to the patient. Still, quite a number of important diagnostic points may be obtained without using the tube, so that it is advisable to employ the other methods of examination first.

THE SIZE AND POSITION OF THE STOMACH

In this connection some of the results of W. His's recent studies, as well as those of Röntgen-ray examination, merit brief mention:

His[1] found, as Luschka had before him, that the empty stomach is not relaxed and does not hang down, but is contracted, so that its size is much reduced and its walls appear thickened. Luschka, however, considered the cardia and the pylorus as points of fixation; but Braun showed (and His has confirmed his findings) that not the pylorus but the second part of the duodenum (pars descendens) is the fixed point, and that, accordingly, as clinical experience with gastric tumors indicates, the pylorus can undergo marked changes in position. The pylorus of an empty stomach lies in the median line; when the organ is filled, it extends further to the right. His states further that, contrary to the older notions, in an empty or almost empty stomach the greater curvature looks somewhat forward, the lesser, toward the spinal column; whereas, when the stomach is filled, the lesser curvature looks upward and the greater downward. The lesser curvature of an empty stomach runs downward and to the right until the pylorus is reached. In complete and moderate filling, on the contrary, the pars pylorica rises upward and to the right from the deepest part of the stomach (His), so that it is not itself the lowermost portion. This formerly much-disputed question, which is of great physiologic significance, has been answered in the same way as above by Röntgen-ray examinations. The female stomach is, according to His, more nearly vertically placed than that of males. The corset stomach of laced women is described by His as a dependent loop with a decided lateral concavity.

Rieder,[2] Grödel,[3] and Holzknecht[4] have recently studied the form, position, and size of the normal stomach with the x-rays after filling the organ with bismuth

[1] Arch. f. Anat. u. Physiol., Anat. Section 1, 1903, p. 345.

[2] Fortschritte auf dem Gebiete der Röntgenstrahlen, viii, 3, Münch. med. Woch., 1904, 35, and ibid., 1906, 3.

[3] Arch. f. klin. Med., 1907, vol. xc, p. 443.

[4] Berl. klin. Woch., 1906, 5.

paste. Both Rieder and Grödel decided that in the erect posture the normal full stomach is fish-hook or siphon shaped. The left half of the filled stomach assumes an almost vertical position, reaching to the level of the umbilicus or below it, and thence turning up sharply to the pylorus (Fig. 199). Grödel found that the upward bend of the stomach disappeared in the recumbent posture (Fig. 199, dotted line). The picture thus approaches Luschka's anatomic representation (see Fig. 120) more closely in recumbency on account of the alteration in the direction of the force of gravity. Grödel is, however, of the opinion that even in this position there is a hook-shaped bend of the stomach, with the difference that the site of the curve is shifted toward the spinal column under the influence of gravity. Only exceptionally (in but 1 of 92 cases and that in a cripple) did Grödel find the pylorus to be the lowermost part of the stomach, although Holzknecht found this to be the rule. Such a state of affairs is, however, unlikely, for physiologic reasons. According to Symmonds, the hook-shaped stomach is found even in the first year of life. Not uncommonly irregularities in the shape of the stomach occur, especially a left-sided

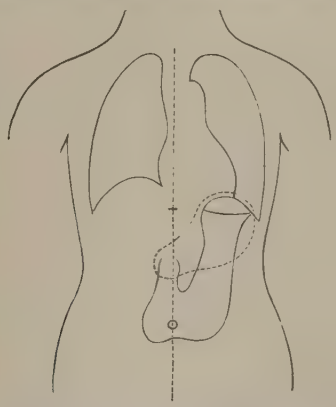


Fig. 199.—Form and position of the normal stomach of a sixteen-year-old youth in the erect (continuous line) and recumbent (dotted line) postures. The part above the transverse line in the first picture is filled with air above the bismuth paste used to distend the stomach. It is called the stomach bladder (bubble) (F. M. Grödel).

hollowing of the vertical part. This is especially frequent in women as a result of tight lacing. The author mentions it because he has known the Röntgen-ray picture of such an abnormal form to lead to the incorrect diagnosis of hour-glass stomach or even of gastric tumor. Grödel's projection pictures do not correspond to the results of inflation and percussion (see p. 424) because, as he was able to show, inflation with air displaces the stomach upward in an abnormal manner, whereas filling the organ with bismuth stretches it downward. The results of percussing the boundaries of the stomach after filling the organ with water or food are, on the other hand, quite comparable to the Röntgen-ray pictures.

METHODS OF EXAMINATION WITHOUT EMPLOYING THE STOMACH-TUBE

The subjective symptoms in the diagnosis of stomach disorders play an important part, *i. e.*, the complaints, the kind of pain or vomiting, and the time when they occur, the character of the stools, etc., in short, the history in the broadest sense of the word. But all this belongs rather to special pathology.

For the objective examination, which chiefly concerns us, the author refers to the sections upon Inspection, Palpation, and Percussion of the Abdomen; but a few special points must be taken up here.

THE DETERMINATION OF THE SIZE, POSITION, AND SHAPE OF THE STOMACH WITHOUT THE USE OF THE SOUND. THE SO-CALLED SPLASHING

It is difficult to estimate the size of the stomach by percussion (see p. 257), but, if the abdominal walls be lax, inspection will often show the outlines of the stomach, the greater and sometimes the lesser curvature as well. Palpation will sometimes permit a differentiation of the tense stomach from the less tense intestines. If these methods of examination afford no definite result, as is frequently the case, we may fill the stomach either with gas or fluid. The former may be accomplished by giving the patient a teaspoonful of sodium bicarbonate, and immediately afterward the same amount of tartaric acid, each salt dissolved in a half-glassful of water. The alkaline solution should always be swallowed first, because the acid solution might cause pain if the mucous membrane be sensitive, and especially if a gastric ulcer be present. The admixture of the two solutions produces carbonic acid gas, which distends the stomach so that its outlines can be easily defined by inspection, palpation, and percussion. If this test be successful, percussion is hardly necessary. The experiment is, however, not always successful, for the stomach may rapidly expel the gas, either upward or downward. Again, a large dilated stomach might require the development of more gas, and so we should have to repeat the attempt with a second and larger dose of effervescing powder. It is not advisable to use too great an amount at first, because it may distend the stomach too much and cause pain. Inflating the stomach with air [by means of an ordinary Davidson syringe.—Ed.] is free from all these disadvantages, and the amount of air can easily be controlled. Distention with gas gives an incorrect picture because it crowds the stomach upward, whereas the ordinary conditions of filling enlarge it downward.

A reasonably accurate estimate of the size of the stomach can be reached in some cases by noting the change in percussion which ensues when the patient, while erect, swallows water little by little. It is best to commence with the fasting stomach, which is usually retracted and entirely covered by intestine. After one or two glassfuls of warm water have been swallowed, the fundus will be dropped downward and forward, and light percussion will bring out an approximately half-moon-shaped dulness in the region of the greater curvature (Fig. 200, *a*). It is perfectly easy to see that this dulness corresponds to the liquid within the stomach, for if the patient swallow more water, the size of the dull area will be increased upward, provided the stomach-wall is of normal resistance (Fig. 200, *b*); but with a lax wall or with a pathologic dilatation of the stomach, the weight of the fluid will depress the greater curvature (Fig. 200, *c*). The same fish-hook or siphon shape of the stomach as *x*-ray examination shows can sometimes be brought out by still greater filling. (See Fig. 199, p. 423.) This method is generally less valuable than inflation with gas; besides, it is annoying and sometimes distressing to the patient, especially so unless moderately warm water is employed.

The dislocation of the spleen in association with gastric dilatation should always be borne in mind. The enlarging stomach draws it downward by means of the gastrosplenic ligament, until it can be readily palpated.

The normal position of the greater curvature, if the stomach be distended with gas, should not be lower than perhaps two fingerbreadths above the navel. (See Fig. 120.) But in estimating the size of the stomach we must remember that the greater curvature is always depressed in gastroptosis, either in the congenital form or especially in that resulting from *enteroptosis*, and also in the marked loop-shaped types; and yet in both these instances the stomach need not be really dilated and its functions may still be normal. Therefore it is advisable to map out the position of the lesser as well as of the greater curvature, and this can be best accomplished by inflating with gas.

The capacity of the stomach varies considerably even under physiologic conditions. This variation depends largely upon the diet, *e. g.*, a person who lives chiefly upon vegetables, such as potatoes, gradually

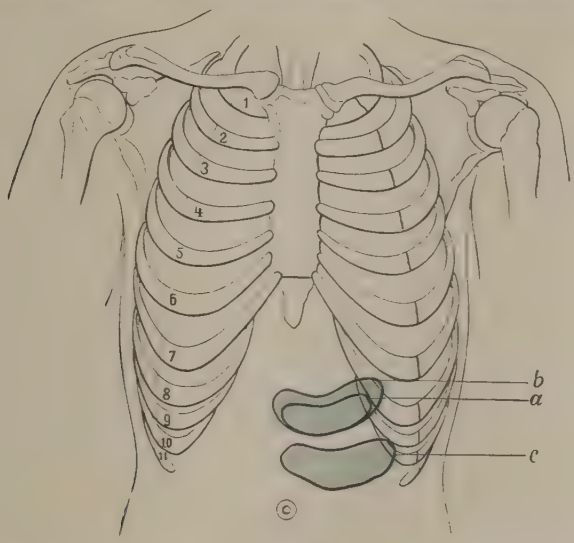


Fig. 200.—Dulness due to liquid in the stomach, percussion in the erect posture: *a*, With a small amount; *b* and *c* with larger amounts; *b*, with normal gastric tone; *c*, with lessened gastric tone, *i. e.*, stretching of the greater curvature by the weight of the fluid.

develops a very large stomach, although it need by no means be diseased. Increased capacity then signifies only a large or an enlarged stomach. Before a stomach can justly be called pathologically enlarged, *i. e.*, a dilated stomach, or, "Stauungsmagen," we must be sure that the enlargement is accompanied by a loss of motility, *i. e.*, by motor insufficiency.

Splashing sounds in the gastric region (see later section upon Gastric Motility), elicited by so-called "dipping" percussion, depend upon the presence of air and fluid. For this purpose the patient is best examined in the dorsal decubitus. With the left hand placed flat upon the epigastrium for palpation, and the ear near the body, the examiner strikes gently with the right hand in the left hypochondrium, or upon the lower left ribs. The splashing may then be felt as well as heard. Splashing sounds do not necessarily mean a dilatation or insufficient motility

unless they are elicited when the stomach should be empty, in the morning before breakfast, or more than seven hours after an ordinary meal. If heard or felt under such circumstances, the sign means motor insufficiency of the stomach, which is most common in pathologic dilatation of the stomach. Again, if the splashing can be obtained over an area larger than the normal (see above), we may consider the organ enlarged.

A very decided splashing sound elicited by quite gentle tapping over the stomach area suggests, however, a gastric atony, even if obtained within the time limits and the area mentioned above. We might call this "superficial splashing," in contrast to "deep splashing" elicited by vigorous blows. This superficial splashing merely shows that the stomach-walls are relaxed (gastric atony), and this may or may not be associated with gastric dilatation. On the other hand, a pathologically dilated stomach, or "Stauungsmagen," need not show any decided signs of atony, *i. e.*, it need not furnish any superficial splashing, especially when the gastric dilatation is due to stenosis of the pylorus. A pathologic dilatation of the stomach which does not lead to a superficial splashing, and conditions of relaxation which do lead to a superficial splashing (*i. e.*, atony) are two fundamentally different lesions, and should be distinguished properly one from the other. The foregoing explanation of the significance of superficial splashing should not be misconstrued, as it has been,[1] for the author does not invariably make a diagnosis of motor insufficiency of the stomach merely from the demonstration of a superficial splashing. Nor does he regard motor insufficiency and atony as identical conditions. By atony he understands merely a diminished tension. Many such *gastric atonies* are never complicated by any other symptoms, and he especially wishes to insist that the length of time that the food remains in the stomach need not be in any way prolonged by mere atony. He considers "atony" diagnostically significant, not as a name of a disease, but merely as a name of the physical condition of the stomach, with which, of course, diseased conditions of the gastric function may, under some circumstances, be combined. So far as the significance of "superficial splashing" is concerned, it should be noted that even relaxed abdominal walls may favor the origin of "superficial splashing," because the tension upon the gastric contents equals the sum of the pressure of the abdominal walls and of the gastric musculature, and because a superficial blow naturally has a stronger action the less the tension of the abdominal walls. From perfectly evident reasons "superficial splashing" will be favored by a low position of the stomach (gastroptosis), quite independent of the usual association of this position with gastric atony. It may still further be noted that the atony of the gastric muscularis may be entirely concealed by pronounced passive tension of the gastric wall due to an abundant meal. Then, despite the atony, the full stomach, up to a certain time, will not furnish any "superficial splashing."

Sometimes a splashing may be wrongly referred to the stomach when it really proceeds from the colon filled with liquid feces and gas, as in some cases of diarrhea. The existence of diarrhea and the demonstration of a similar splashing along the ascending and descending colon will usually prevent any confusion. Splashing may also come from the small intestines and yet be perfectly normal.

[1] Elsner, Berlin. klin. Woch., 1901, No. 16.

Neurasthenics and hypochondriacs sometimes consult their physicians in regard to a splashing sound which they produce themselves in the gastric region by contracting and retracting their abdominal walls. This sound may be a true splashing, but it is important only when it occurs under the conditions mentioned above. It may be produced when the stomach is quite normal and nearly empty by an alternate separation and rubbing together of the stomach or the intestinal walls.

EXAMINATION OF THE GASTRIC FUNCTIONS WITHOUT THE USE OF THE STOMACH-TUBE

The functions of the stomach are: (1) Digestive, (2) receptive, and (3) antiseptic. In the first place, it chemically alters proteins and carbohydrates and thereby facilitates and aids in their resorption. In the second place, it acts as a well-equipped reservoir, and at the proper time supplies properly prepared food for the intestines to digest completely and to assimilate. With this assistance it is possible to ingest our food at a few definite periods, meal-times, and during the intervals to devote ourselves to other interests. In the third place, it protects the intestines from the injurious action of the noxious micro-organisms contained in the food. Hence we must study not only the chemistry of gastric digestion and the power of absorption of the gastric walls, but also determine its motility and its germicidal function.

EXAMINATION OF THE VOMITUS

Considerable information about the chemistry of digestion may be acquired from carefully examining the vomitus. Even a macroscopic examination will enable us to draw valuable conclusions, especially in regard to the digestion of meat, if the vomiting occur during the time when the digestion ought to be pretty well advanced physiologically. If we find bits of unchanged meat or albumin in the material vomited two to three hours after eating, we are justified in assuming some disturbance of protein digestion. The changes of other kinds of food in the stomach are less characteristic. Bread, however, should be altered within one to two hours after ingestion to a uniform mass of purée-like consistence, which settles as a granular layer at the bottom when the vomitus is allowed to stand. If the vomitus at this interval contain crumbs of unaltered bread, perhaps covered with mucus, we are usually justified in assuming disturbed protein digestion, depending generally upon a deficient secretion of hydrochloric acid. We may also employ a dilute iodin solution to determine the degree of amyloid digestion. This will be described later in connection with the Test-breakfast (p. 448 et seq.). But we must remember that after the completion of normal gastric digestion we still find in the stomach-contents microscopically numerous, apparently intact, meat-shreds and starch-granules. Hence, very little dependence can be placed upon the microscopic examination of the vomitus. The vomitus should, therefore, be subjected to the same chemical tests to be described later for the expressed test-breakfast. The results will, however, not be very valuable, because gastric digestion varies markedly with the character of the food ingested and the length of time since ingestion. Free hydrochloric acid should, nevertheless, be found in the gastric juice within one to two hours after

eating an ordinary meal; and the filtrate from the vomitus should digest fibrin or coagulated albumin.

Furthermore, the examination of the vomitus may give some conclusions about the gastric motility. If an individual vomit bits of food more than seven hours after a meal, some impairment of motility must exist, for after that interval even a hearty meal should have completely left the stomach. If this late vomiting be very noticeable, or if, perhaps, a larger amount be vomited than was ingested at the last meal, a very pronounced motor insufficiency, usually associated with *extreme gastric dilatation,* may be assumed. If the vomitus contain particles of

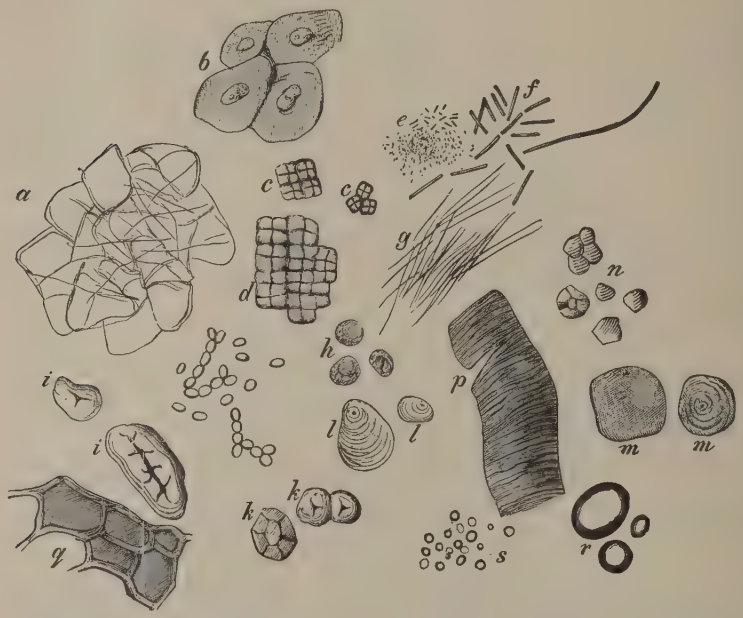


Fig. 201.—Microscopic constituents of vomitus: *a*, Fragment of an apple (crushed); *b*, pavement epithelium; *c*, Sarcina ventriculi (smaller type); *d*, Sarcina ventriculi (larger type); *e*, bacterial clump; *f*, large bacilli (Boas-Oppler bacilli, B. geniculatus) which are frequently found in the vomitus from gastric carcinoma; *g*, needles of fatty acids; *h*, white blood-corpuscles; *i*, vegetable starch; *k*, corn-starch; *l*, potato starch; *m*, white-bread starch; *n*, rice starch; *o*, yeast-cells; *p*, muscle-fibers; *q*, vegetable tissue; *r*, fat-drops; *s*, milk or cream drops.

food known to have been ingested at some previous meal or a day or two before (seeds of fruit, etc.), such a diagnosis becomes certain.

If we can show that the excess of the vomitus over what was ingested at the last meal consists largely of a thin acid liquid containing free hydrochloric acid, we are entitled to assume a *hypersecretion* of gastric juice. The vomiting of an acid liquid without food-particles from a fasting stomach is especially characteristic of this condition. In the latter case the secretion of the gastric juice apparently does not depend upon the ingestion of food, but occurs continually (*hypersecretion, gastrosuccorrhea*). We must, however, remember that in some of these cases, and perhaps in the majority, the hypersecretion is due entirely to a motor insufficiency, *i. e.*, to the fact that secretion

is continually excited in a stomach which never empties itself completely. In contrast to these cases of hypersecretion in the strict sense, there are others characterized as *simple hyperacidity*, in which the vomitus is not abnormally abundant, but is abnormally and intensely acid (due to free hydrochloric acid). The method of determining this is by titrating the filtrate for its acidity. It will be described later. A quantitative comparison with the normal is, however, justifiable only when the vomiting occurred one or two hours after the meal, and when longer-retained food portions are not mixed with the vomitus. It was formerly assumed that both the motility of the stomach and its power of absorption are affected if a considerable quantity of a fluid which makes no demands upon digestion, such as water, coffee, etc., be vomited several hours after ingestion, and if the acidity of the fluid do not indicate hypersecretion. For it was claimed that, physiologically, the absorp-

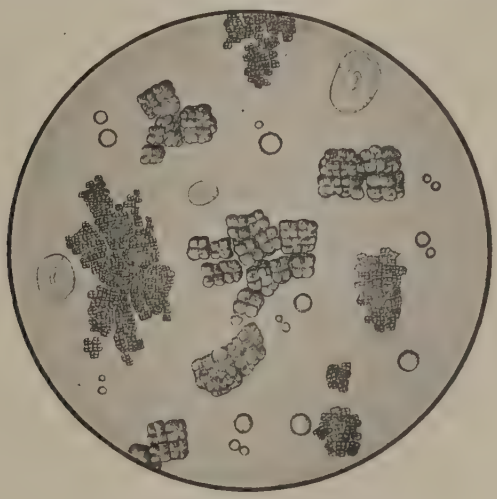


Fig. 202.—Gastric contents from a case of benign pyloric stenosis. Sarcina ventriculi, large and small forms, fat-drops, and starch-granules.

tion even of large amounts of fluids by the stomach is exceedingly rapid. But von Mering's investigations show that under physiologic conditions the stomach absorbs hardly any water, so that the latter factor seems incorrect, and therefore we must attribute the retention of fluids as due to *deficient motility* alone.

An examination of the vomitus gives us important information about the *antiseptic qualities* of the gastric juice. Decomposition in the gastric contents depends either upon a diminution in the amount of hydrochloric acid contained in the secretion (for the acid acts as an antiseptic) or upon stagnation of the gastric contents, *i. e.*, upon some interference with the motility of the stomach. The vomitus is then apt to be foamy and to smell of some of the volatile fatty acids (butyric acid, acetic acid, p. 452), or to have some other disagreeable odor; and microscopically we find abundant micro-organisms, especially Sarcina ventriculi, yeast fungi, cocci, and bacilli (Fig. 201). This con-

dition is most pronounced in a dilatation of the stomach due to stenosis, especially from carcinoma of the pylorus, where the food often stagnates in the stomach as a result of mechanical obstruction for several days. We frequently find in carcinoma of the stomach, and more rarely in gastric dilatation due to other causes, peculiar thin bacilli, sometimes arranged in long threads (Boas-Oppler bacillus, Bacillus geniculatus, and Bacteriologic Examination of the Gastric Contents)[1] (Fig. 201). Cocci and bacilli are usually found in larger quantities in gastric juice which is poor in hydrochloric acid; whereas sarcinæ and yeast fungi may flourish in gastric juice rich in hydrochloric acid. We meet with two types of gastrosuccorrhea (*continuous hypersecretion of gastric juice*). In both, the stomach always contains material with free hydrochloric acid, and this is apt to be vomited from time to time. In *the milder type* this material is free from micro-organisms. In *the more severe type* the large amount of hydrochloric acid present is no longer capable of keeping the stomach-contents aseptic, but micro-organisms grow abundantly, owing to the high degree of motor insufficiency. In this case chiefly yeast fungi and sarcinæ are found in the vomitus, and may be present in abundance even with 0.3 per cent. HCl.

It must be noted that bread itself contains greater or less numbers of bacteria and yeast-cells. Hence, before conclusions are justified, the bacteriologic examination of the gastric contents after the ingestion of bread should first be compared with a similar examination of the bread.

Abundant tough, slimy masses in the vomitus indicate a mucous catarrh of the stomach or a diminution in the hydrochloric acid, for under normal conditions the mucus produced by the mucous membrane is in part digested. (Compare later Examination of the Mucous Secretion of the Stomach.) An *admixture of blood* may be found in the vomitus under many different conditions. A slight, streak-like admixture of blood in the vomitus is of no diagnostic importance whatsoever, for the violent act of vomiting may produce some slight mechanical lesion of the stomach, esophagus, or pharynx. An abundant admixture of fresh arterial blood or of blood stained dark and coagulated by the acid gastric juice is especially suggestive of ulcer of the stomach. Cirrhosis of the liver is also responsible for profuse gastric hemorrhage. Brown or black material resembling coffee-grounds, if granular and intimately mixed with the stomach-contents, is suggestive of gastric carcinoma; but the same condition frequently results from hemorrhagic erosions of the gastric mucous membrane, especially if associated with hyperacidity or hypersecretion. We can prove that this appearance is due to the altered blood by microscopic or spectroscopic examination, or by Teichmann's test.[2] (See under Urine, p. 573.)

Pus may be found in the vomitus, due to the very rare condition, *suppurative* or *phlegmonous gastritis*. *Admixture of bile* produces a yellow or greenish discoloration of the vomitus. In a doubtful case we can apply Gmelin's test for biliary pigment. (See Examination of the Urine, p. 575 et seq.) Admixture of bile may occur with any type of vomiting, for the contents of the duodenum may be forced into the stomach

[1] Sandberg, Zeit. f. klin. Med., 1904, vol. li; also Palier, Presse méd., 1906.

[2] The author recommends the modification of the turpentine-guaiacum, aloin or benzidin tests described under Examination of the Feces for Blood.

mechanically by the act of vomiting. It is, however, observed most frequently in vomiting from the fasting stomach, perhaps because there is then no counterpressure from gastric contents to prevent the regurgitation from the duodenum. For the same reason biliary vomiting occurs in duodenal stenosis. The vomitus of *cerebral meningitis* is less apt to be mixed with bile, because these patients still take considerable nourishment, and the vomiting generally starts with a partially filled stomach, *i. e.*, the vomiting in this disease is both peripheral and cerebral in origin. Green biliary vomitus is, of course, by no means pathognomonic of peritonitis.

Fecal vomiting is a characteristic sign of complete motor insufficiency of the intestines (in peritonitis), or of *intestinal obstruction* in the lower part of the small intestine or in the large intestine. The odor and brownish color of the vomitus are distinctive. Microscopically, it is found to contain large numbers of bacteria. *Cholera nostras* and *cholera Asiatica* are characterized by the vomiting of abundant *alkaline rice-water-like* material (exactly like the cholera stools). It usually contains whitish shreds of mucus. In cholera Asiatica, the comma bacillus (Koch) (see Examination of Feces) may be found in the vomitus. We are not yet certain about the organism of cholera nostras. The Finkler-Prior comma bacillus, the colon bacillus, various forms of the proteus group, and streptococci (see Pathognomonic Bacteria of the Feces) have all been found in the feces, and also in the vomitus of cholera nostras. The occurrence of streptococci in the vomitus has assumed some importance recently in the etiologic diagnosis of other gastro-intestinal infections. (See later Pathogenic Bacteria of the Feces.)

The color, odor, and chemical examination of the vomitus may sometimes aid in tracing the occurrence of stomach disturbance to some sort of poisoning (prussic acid, alcohol, etc.). In uremia the vomitus often possesses the odor of ammonia, for the urea eliminated in the stomach-contents may be converted into carbonate of ammonia while still in the stomach. (See note on p. 498 for the demonstration of poisons in the vomitus.)

Intestinal worms, more especially ascarides, are sometimes found in the vomitus. (See later, Animal Parasites in the Stools.)

It is sometimes difficult to decide whether food particles which the patient expels from the mouth come from the stomach itself, or whether they are only regurgitated from the esophagus (*diverticulum from stenosis of the esophagus*). The presence of free hydrochloric acid will generally settle the doubt.

EXAMINATION OF THE POWER OF ABSORPTION OF THE GASTRIC MUCOUS MEMBRANE BY MEANS OF POTASSIC IODID

Penzoldt and Faber[1] have published a direct method of testing the absorbing power of the gastric mucous membrane. The procedure depends upon the principle that, under physiologic conditions, potassic iodid is very rapidly absorbed by the gastric mucous membrane and then eliminated immediately in the saliva. The length of time from the ingestion of the potassic iodid until the saliva exhibits a distinct iodin reaction may be considered as a measure of the rapidity of absorption, provided that slight differences in the time of elimination be neglected. The potash is administered in a gelatin capsule filled carefully enough to avoid any particles of the salt sticking to the outside, and so liable to be absorbed by the mouth or esophagus.

[1] Penzoldt and Faber, Berlin. klin. Woch., 1882; Zweifel, Deut. Arch. f. klin. Med., vol. xxxix.

To demonstrate the iodin, the patient spits upon the edge of a white plate, a little starch powder is added to the saliva, and then, while it is being stirred carefully, 1 cc. of dilute sulphuric acid and a drop of 1 per cent. sodium nitrite solution are added. The nitrous acid sets iodin free from the potassic iodid in the saliva and produces the well-known violet color (starch iodid). Any excess of acid will oxidize the iodin to iodic acid, which does not give this violet color. The acid should, therefore, be added drop by drop and stirred. The reaction is less sensitive if the saliva remain any length of time in contact with the starch, because the saliva changes the starch to erythrodextrin and achroödextrin. If these substances unite with the iodin, colorless or only pinkish combinations result; hence the admixture should be made promptly. If a few drops of chloroform be added to the saliva before adding the acid, the chloroform will dissolve the free iodin and produce a rose color. Sulphuric is now recommended instead of nitric acid because the latter frequently contains iodin.

Experience shows that under normal conditions the first trace of iodin appears in the saliva ten or more minutes after the administration of 0.1 gm. potassic iodid upon an empty stomach. If, however, the stomach be full, or if food be given simultaneously with the drug, the absorption and test will be delayed. Hence the experiment should always be performed either upon an empty stomach or coincidentally with a test-breakfast. Bauer, in the Bern Clinic, found, from a series of experiments, that if the drug were taken with an Ewald test-breakfast, the reaction appeared in the saliva, under normal conditions, in from five to twenty minutes. If retention be suspected, the stomach should, of course, be first washed out. If the reaction be delayed, although the stomach is supposed to be empty, retention is the probable cause, because experience shows that there is rarely much retardation of the reaction in an absolutely empty stomach, even under pathologic conditions.

Of course, this method does not give any information as to the absorption of food substances, for, as a matter of fact, potassic iodid, even under the most unfavorable pathologic conditions, is absorbed with ease.

If v. Mering's[1] experiments be confirmed, this method becomes entirely useless. He finds in dogs, and very likely the same is true in men, that potassic iodid is not absorbed at all from the stomach, not even within one or two hours. Hence we must acknowledge that the rapid appearance of the iodin reaction in the saliva depends upon the absorption of the iodid in the intestines, and is in reality only a measure of the gastric motility. However, von Mering's results have recently been called into question by Boas.[2]

EXAMINATION OF THE MOTILITY OF THE STOMACH WITHOUT THE USE OF THE STOMACH-TUBE

Palpation (p. 426 et seq.), especially eliciting the splashing sound of the stomach, gives us some idea of the gastric motility; so too does the examination of the vomitus (p. 427 et seq.). Ewald and Sievers and then Huber recommended the employment of salol to test the motility. Salol or salicylate of phenol passes through the stomach unchanged, and splits up only after it reaches the intestine into salicylic acid and phenol, under the influence of the pancreatic juice and the intestinal bacteria. Salicylic acid, soon after absorption, is eliminated in the urine as salicyluric acid (ferric chlorid produces a violet color when added to the urine; see Examination of the Urine). Assuming that the salol is always broken up with equal rapidity, this reaction should measure the rapidity with which it reaches the intestines; in other words, the gastric motility.

Ewald and Sievers administer the drug with the test-breakfast; then the patient urinates at regular intervals during the next few hours, and the ferric chlorid test is performed upon each specimen. Normally, the salicyluric reaction occurs within seventy-five minutes. If delayed beyond this period, Ewald considers that motor insufficiency may be diagnosed.

This method of testing is beset with a number of errors. The most important one is that we can never be sure whether the movements of the stomach produce a uniform mixture of the salol and stomach-contents, so that whether the salol leaves the stomach with the first portion of the food mass or later on must largely depend upon chance. Hence the salol should be intimately mixed with the food, or else taken in small portions (as an emulsion in water) during the meal. The rapidity

[1] Klin. Jahrb., 1899, vol. vii; also Boas, Arch. f. klin. Med., 1904, vol. lxxxi, 456.
[2] Arch. klin. med., 1904, lxxxi, 5 and 6, p. 456.

of splitting up, of absorption, and of elimination is not always a definitely fixed and constant quantity. The author's investigations with glutoid capsules have shown that great variations in the intensity of proteolytic action of the pancreatic juice occur. However, in spite of these sources of error, the method gives quite reliable information regarding the more pronounced disorders. In marked gastric retention all the salol may remain for hours in the stomach.[1]

Huber modified this method by determining the length of time which elapses before all the salicyluric acid is excreted. The reasoning is clear. The moment of the appearance of the salicyluric acid reaction depends principally upon the rapidity with which the stomach passes the first amount of salol into the intestine; but the persistence of the reaction in the urine (assuming rapid splitting up and rapid elimination of the salol in the intestines) is due to the fact that the stomach has not yet passed on all the salol. Therefore the duration of the salicyluric acid reaction may be a better measure of stomach motility than the period of its first appearance. Huber's investigations have shown that in healthy individuals who have taken 1 gm. of salol at a meal the salicyluric reaction has always disappeared inside of twenty-six or twenty-seven hours. Motor insufficiency may therefore be assumed if this time be exceeded. With this method the urine need not be tested until about twenty-seven hours after taking the salol. Of course, the urine should be voided a little beforehand, *e. g.*, one-half hour, so that no residual urine remains. If the salicyluric reaction be present twenty-seven hours after the ingestion of the salol, the test should be repeated every three hours until it disappears. The degree of motor insufficiency is in direct proportion to the duration of the reaction.

Ewald's and Huber's methods may be combined as follows: 1 gm. of salol is taken with the meal, either intimately mixed or in very small quantities, and then the time of appearance and of disappearance of the salicyluric acid in the urine is noted.

The salol tests will reveal impairment of motility in all sorts of stomach disorders. The appearance of the reaction may be delayed for several hours, and not infrequently it persists for forty hours or more.

Iodipin has recently been recommended by Winkler and Stein instead of salol. Iodin is set free and absorbed in the intestines and then tested for in the saliva or urine. A quarter to a half hour after a test-breakfast the patient is given a small teaspoonful of iodipin containing 10 per cent. of iodin, and the urine or saliva is examined every fifteen minutes for iodin. Normally, iodin reappears in from sixty to seventy-five minutes. Fleischer has also used iodoform for a similar purpose (capsule containing 0.1 gm. of iodoform). The iodin reaction in the urine and saliva appears normally at the latest in one and three-quarter hours. The examination of the urine is more certain than that of the saliva. (See p. 507.)

The author is convinced that none of these methods is perfectly trustworthy for estimating the gastric motility. In the first place, we are not sure that the substances employed are intimately mixed with the gastric contents, nor are we certain that they may not be precipitated by the gastric juice and reach the intestines too soon or too late. Again, the results will be very decidedly influenced by the rapidity of the splitting up and of the absorption in the intestines. If von Mering's idea be confirmed (see p. 432), that potassic iodid is not absorbed at all in the stomach, then Penzoldt and Faber's method for testing the absorption in the stomach can be utilized as a test of its motility (p. 431 et seq.). Further investigations upon the point are necessary.

TESTING THE DIGESTION WITH POTASSIC IODID FIBRIN—RUBBER CAPSULES

Although this method was detailed at length in a previous edition of this book, it has since led to no practically useful results, and so it need only be alluded to.

THE DESMOID TEST

In the Correspondenzblatt für Schweizer Aerzte, No. 8 and 9, 1905, the author described a method which was based on the fact, discovered by Kühne and Schmidt, that *raw* connective tissue is not attacked by the digestive ferments of the intestine

[1] There is, however, reason to believe that in cases of grave disturbances of motility, when the salol remains for hours in the stomach, some of the drug may also be absorbed by this organ. Part of it is, perhaps, first split up by micro-organisms, which are rarely absent in a stagnant stomach, or by the fat-splitting ferment of the stomach. Such a slow absorption, however, would rarely, if ever, lead us to assume that the motility was normal.

but is dissolved in the gastric juice. This test was called the *desmoid reaction.* With this test one may arrive at certain conclusions regarding the functional capacity of the stomach without the aid of a stomach-tube, naturally not superseding the use of this instrument from the diagnostic armamentarium. The principle of the reaction is similar to that of the glutoid test, in the determination of the resorption and excretion of a substance contained, either in a membrane of gold-beater's skin or in caoutchouc, after its liberation from its capsule. The indicators used are either iodoform, the iodin of which is detected in the saliva or in the urine, or methylene-blue, which may be excreted in the urine as the coloring-matter itself or as the colorless chromogen. If one of these small containers be taken with a meal, the normal gastric juice will dissolve the connective tissue with which the sac is tied and liberate the indicator. The latter will be absorbed and excreted.

Preliminary trials showed that catgut or gold-beater's skin is not dissolved by trypsin or by putrefactive processes. Preliminary treatment of these tissues with pepsin-hydrochloric acid, short of solution, does not render them soluble in trypsin. Clinical experiments showed that neither the succus entericus nor pancreatic juice was capable of acting upon them. Catgut is selected because it lends itself better to the test than the gold-beater's skin.

The materials used in the test are the following:

(1) Rubber membrane of the finest Para rubber, the dental dam of commerce. This membrane is 0.2 mm. thick, and can be obtained from E. Doherty, 110 Kent Avenue, Brooklyn, N. Y. The membrane is light in color. It is best to use the product of the above-mentioned firm for the test.

(2) Catgut of the finest quality, 0.3 mm. thick.

(3) Pills made exactly after the following formula. The pills must be dried perfectly hard and subsequently dusted with lycopodium:

(*a*)	Iodoform	5.0 gm.
	Ext. glycyrrhizæ	2.0 gm
	Pulv. glycyrrhizæ	2.0 gm.

Divide into 50 pills.

(*b*)	Methylene-blue (medicinal)	2.5 gm.
	Ext. glycyrrhizæ	2.0 gm.
	Pulv. glycyrrhizæ	2.0 gm.

Divide into 50 pills.

More recently the author has used pills which are heavier than the above, and which sink at once in the stomach-contents.

They are composed as follows:

(*a*)	Iodoform	20.0 gm.
	Pulv. glycyrrhizæ	10.0 gm.
	Bismuth. subnitratis	100.0 gm.
	Glucose syrup (sat'd)	q. s.

Divide into 200 pills.

(*b*)	Methylene-blue (medicinal)	10.0 gm.
	Pulv. glycyrrhizæ	10.0 gm.
	Bismuth. subnitrat	100.0 gm.
	Glucose syrup (sat'd)	q. s.

Divide into 200 pills.

These pills are hygroscopic and must be kept in a dry place. The sacs in which these pills are placed must be prepared fresh each time they are used.

Preparation of the Desmoid Sacs.—A piece of the membrane, 20 cm. square, is immersed in water until it is soft, then removed, and dried thoroughly. The worker's hands must also be quite dry. From this a piece of membrane 4 cm. square is cut out and sprinkled with talcum powder. The pill is then laid in the center of the square and the corners taken up. The membrane must not be stretched. The pill is then included completely in the membrane by twisting the ends in a clockwise direction. (See Fig. 203.) The torsion employed must not be too great. When the twisted portion of the sac is tightly held by the thumb and forefinger of the left hand, the right hand may be released. The next manipulation is to tie the sac with catgut. This requires a little practice. One end of the catgut is placed under the left thumb, and the catgut wound three times round the neck of the sac in a clockwise direction. This is done to prevent burying the strands of the catgut in the rubber, and so pre-

venting contact with the gastric juice. At the same time the winding must be done in such a way as to avoid the further stretching of or cutting the india-rubber. The catgut is finally secured by a double knot. Both knots must be on the same side of the neck, else in order to loosen the neck the digestive action must occur at both knots. (See Fig. 203.) The rest of the dental membrane is cut away at a distance of 3 to 5 mm. from the ligature. It is better not to cut the free end of the rubber in one cut, but to take a single layer and gradually cut it away. In this way one avoids sealing two layers of the rubber together by pressure from the scissors. The sacs sink in water, and leave the stomach with the last portions of the meal. It is well to ascertain whether they actually sink in water or not. If they do not, the rubber may be cut a little closer to the ligature. The bismuth pills sink in a fairly thick chyme, especially if they be taken immediately after soup. The sacs must be perfectly water-tight. Those containing methylene-blue must not release any of the coloring-matter when allowed to stand in water at body temperature for twenty-four hours.

Method of Use.—The practical details of using the sacs are as follows: Immediately after soup at lunch the patient swallows the sac with the aid of a little water. It is not advisable to inclose the sac in a gelatin capsule, for the air in the capsule will

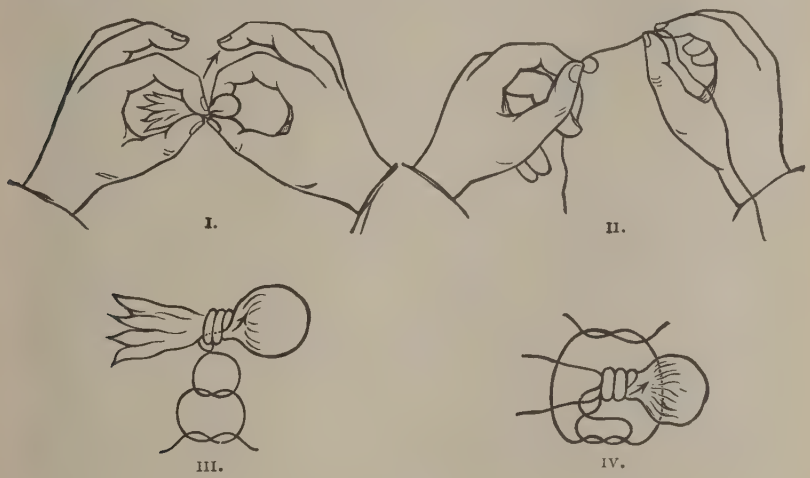


Fig. 203.

allow it to float. The pills can be used one after the other, if the methylene-blue pill be used first. The detection of iodin in the urine is not disturbed by the presence of methylene-blue. The sacs must be swallowed carefully in order to prevent their rupture by any untoward movements of mastication. In swallowing them it is better for the patient to hold the head well back. The patient may now go about, but in those confined to bed it is necessary to caution them not to lie on the right side, for in that case, in consequence of the high specific gravity of the sac, it is not brought into contact with the gastric juice before it reaches the pylorus.

The patient is told to urinate at 5 P.M., at 7 P.M., and on rising the next morning. These three samples of urine must be collected separately. The elimination of the methylene-blue may be seen immediately by the color it imparts to the urine. In case the urine is not colored, the chromogen, if present, may be converted into the coloring-matter by boiling 10 cc. of the urine with 1 cc. of acetic acid for two minutes. The presence of the chromogen has the same significance as that of the coloring-matter itself.

A positive reaction is obtained when the methylene-blue or the iodin appears in the urine of the same evening or the morning following. Otherwise the test is negative. To test for iodin the urine is first shaken with animal charcoal, after heat-

ing gently, in order to remove the coloring-matter and the chromogen. The charcoal is filtered off, leaving the urine practically colorless. The color may also be removed by the addition of a little calcium chlorid and sodium carbonate, as in Huppert's test for bile-pigments. To detect the iodin, 1 cc. of dilute sulphuric acid and 0.5 cc. of a 1 per cent. solution of sodium nitrite are added to 10 cc. of the urine. To this 2 cc. of chloroform are added. If iodin be present, a rose color will be imparted to the chloroform.

Significance of the Result.—A positive result, the appearance of methylene-blue or iodin in the urine of the same evening or the following morning, indicates that digestion with pepsin-hydrochloric acid occurred in a normal manner. In spite of all statements to the contrary, the author maintains that this is correct. If the sacs be made properly, the catgut is not dissolved either by pancreatic juice or by intestinal putrefaction. The method allows one to determine perfectly whether food, taken at the same time as the sac, has been subjected to normal digestion in the stomach. Further on, the author will discuss the question as to whether the diagnostic conclusions are based on a safe foundation. Experiments have lately been performed with the desmoid test, and it has been found that extremely active preparations of trypsin in soda solutions, ranging in concentrations of from 0.2 to 2.0 per cent., did not dissolve the catgut in several days. In weak solutions of sodium carbonate, in spite of very active putrefaction, the catgut was perfectly resistant. In solutions of 2 per cent. sodium carbonate the catgut commenced to disintegrate after four days. In pancreatin solutions with soda, in which putrefactive processes were prevented by the addition of chloroform, the catgut remained intact for two months. In pepsin-hydrochloric acid it dissolved in a few hours. These experiments have been confirmed on rabbits by M. Gentzen. This investigator placed desmoid sacs in the region of the pylorus or in the intestine after ligating off the stomach, and found that the catgut was not dissolved. The experiments of Saito, who claims that catgut is slowly dissolved in a mixture of pancreatic juice and intestinal extract, are absolutely unconvincing, if he concludes that pancreatic juice activated by intestinal extract is capable of acting on the catgut. Intestinal extract is not comparable to intestinal juice. The ferments of the intestinal tract do not play a part in the solution of the gut. That raw connective tissue is not dissolved by intestinal secretions is seen in Schmidt's meat test, and also in Wölfer's experiments. They are also confirmed by the fact that in achylia the test is, without exception, negative.

A negative test proves that sufficient gastric digestion has not occurred, which may depend either on a deficiency in the gastric digestion or on a condition of hypermotility of the stomach, in which latter case the sac has been removed too rapidly from the stomach.

A delayed reaction, occurring in the afternoon or the evening of the following day, shows that gastric digestion is incomplete. This can occur only when the motility of the stomach is interfered with, as in certain cases of gastric stasis with hypoacidity. The writer has been able to show that in healthy subjects the reaction always occurs in the afternoon or evening of the day on which the sac was given. In diseases of the stomach the following observations were made. It was anticipated at first that the desmoid reaction would indicate whether free hydrochloric acid be present after the ingestion of a meal, and that a positive test would indicate the presence of free hydrochloric acid. This, however, is not always the case. On the one hand, cases occur where free hydrochloric acid is absent and the desmoid test is positive, and the reverse also occurs. At the outset, the author was inclined to attribute these inconsistencies to a fundamental error in the method. At the present time he concludes that they show the insufficiency of the present methods for the examination of the contents of the stomach and the true value of the desmoid test. The grounds for these apparent inconsistencies are the following: The ordinary test-meal is an arbitrary one, and at the same time is not a very severe test for functional capacity, and it cannot be said that the acidity of the stomach-contents will be the same in this test as after a meal more suited to excite the functions of the stomach to their full extent. The author has satisfied himself that usually in those cases where the desmoid reaction is positive, and no reaction for free hydrochloric acid could be obtained after the ordinary test-meal, free hydrochloric acid could be found in the gastric juice three hours after the ingestion of an ordinary meal. Moreover, the total acidity is greater than that in a test-meal, no matter whether the test-meal be that of Ewald-Boas or the flour-soup suggested by the author for the butyrometric test. The desmoid reaction is done under normal conditions with an ordinary meal, while the test-meal is a much less effective gastric stimulus. Aside from this, the digestion may proceed, even in the absence of free hydrochloric acid, for a slow

digestion of albumin has been observed in Mett's tubes when all the free hydrochloric acid was combined with albumoses, and the mixture did not react to Congo-paper. The only condition necessary is that the total acidity must not be too low and the content in albumoses too high. With low acidity and much albumoses, albumin will scarcely be dissolved in vitro. It must, however, be pointed out that in this test the acid is taken up directly from the gastric juice, while with the desmoid test, the small sac, on account of its high gravity, comes into direct contact with the secreting wall of the stomach. The conditions are, therefore, much more normal than any test-tube examination. Further, one must remember that any investigation contingent on siphonage concerns the contents only at a particular time, and the result may be quite different from what might have been obtained before or after that time. All these possibilities must be borne in mind, but the principal one, in the judgment of the author, is due to the great difference in the quality of the two test-meals. The desmoid test is given with an ordinary meal, which favors the production of hydrochloric acid. This is not the case with the usual test-meal. These investigations show clearly how imperfect is our knowledge, with the best of the diagnostic tests for examination of the functions of the stomach, the butyrometric test not excepted. The presence of hydrochloric acid in the gastric contents is due to many adventitious factors, and also to the rapidity with which the chemical conditions change in the organ. It is, therefore, an important fact that in the desmoid test we possess a means of investigating the gastric digestion under strictly normal conditions. The fact that even in the presence of free hydrochloric acid the test sometimes fails is easy to explain. Either the amount of acid is not sufficient for the digestion of the larger meal, the pepsin is not in the proper amount, or it may be that the motility of the stomach is excessive. This last condition indicates insufficient gastric digestion, although the secretion itself is amply active, because the contents of the stomach are not retained in the organ for the proper length of time. An interesting illustration of the latter condition was afforded by a case of hyperacidity and gastric stasis operated on for a cicatricial stenosis of the pylorus. The patient was not benefited by the operation, although obviously the stenosis had been removed. The desmoid test was negative, showing that the sac, in consequence of its high specific gravity, had fallen to the lower part of the stomach, and had been projected with great rapidity into the intestines, and thus had escaped the action of the gastric juice. There was, therefore, besides the beneficial effects of the gastro-enterostomy, an elimination of the physiologic effects of sedimentation in the stomach, a factor which has been so clearly pointed out by Moritz. The condition of the patient was, therefore, not improved by the operation. This fact must be taken into account very seriously in any contemplated operation for gastro-enterostomy. In the event of any indication which is not perfectly clear the operation should be postponed. The desmoid test shows that gastric digestion cannot be entirely replaced by intestinal digestion, as is very often supposed, and it is quite impossible to say beforehand what the effects of gastro-enterostomy may be. The author does not bring these facts forward to minimize the importance of the operation where it is really indicated, as, for example, in severe partial mechanic occlusion of the pylorus, but only to show how insufficient is the basis for assuming that gastro-enterostomy is a harmless panacea for all possible disturbances of the stomach, either due to neurasthenic conditions or true new-growths of the organ.

From the standpoint of practical diagnosis, the desmoid reaction appears to be useful in those groups of cases where the investigation of the gastric contents shows no hydrochloric acid, simple cases, as distinguished from those in which the absence of hydrochloric acid is connected with pernicious anemia or gastric carcinoma. The former cases are recognized by the fall in the total acidity. In the less severe cases of the latter group the desmoid test may be positive in spite of the fact that no hydrochloric acid is found after a test-meal. This is due to the stronger stimulus of the ordinary meal. In the severe cases the test is negative, because the strongest stimulus is incapable of evoking the secretion of pepsin and hydrochloric acid. The author believes that the desmoid test affords a better indication of the functional capacity of the stomach than the detection of free hydrochloric acid. In any case, it appears that the estimation of the total acidity and the amount of pepsin should be given a more important place than is usually done. The desmoid test enlarges our conceptions of the functional capacity of the stomach, through the differences which have been found when comparing this test with the others commonly employed. The latter have often been found to be erroneous.

Important in a physiologic sense are those cases which, in spite of conditions of retention, give a delayed reaction. These cases give an interesting confirmation of the results of Moritz regarding the stomach as a retaining mechanism. He showed

that substances difficult to digest, provided they were of high specific gravity, might be retained in the stomach for a considerable length of time. A rapid transfer of the sac to the intestine would give a negative test. The test is, therefore, a direct demonstration of the teleologically important function of the stomach in the digestion of food, by reason of its capacity for retaining and sedimenting it. It also shows that in gastric insufficiency the stomach may retain food for a considerable length of time in order to complete its digestion, while in chemical inefficiency of a high grade, such as is encountered in pernicious anemia, the stomach is usually more than normally motile, as if by instinct it reacts to the feeling that nothing may be accomplished by the retention of the food in the organ.

The author also wishes to point out that the desmoid reaction is able to indicate anomalies of the digestive function of the stomach, which are not possible to demonstrate with ordinary methods, for neither the pepsin estimation nor the estimation of the acidity gives us results which enable us to distinguish the finer degrees in the disturbances of gastric digestion.

In order not to be misunderstood regarding the relative importance of the desmoid test, it should be said that the test is not only one which indicates the digestive capacity of the gastric juice on connective tissue, which is the most difficult task the stomach has to perform, but, at the same time, it gives an indication of the effect on the meal itself. This is indicated from the fact that those conditions in which the meal is well digested give a positive test, and the converse must also be true, for the action of the digestive juice must be equal on the catgut and the meal.

To this extent, the author believes that one has, in the desmoid test, a method of testing gastric efficiency under normal conditions which has heretofore been impossible. Furthermore, it is possible also to obtain important information regarding the quality of a meal suitable to provoke the necessary gastric secretion.

In conclusion, it may be said that the desmoid test is capable of enlarging our views on the physiology and pathology of gastric digestion, because it alone, of all the tests, permits us to examine the chemical processes of the stomach under normal conditions.

If the author may be allowed to consider certain of the objections which have been raised against the method, he wishes to point out that they concern the differences which have been found between the results of the desmoid reaction and those obtained with a test-meal. The greater number of writers on the subject have not read the author's original papers, and do not understand how he has explained these differences, and has shown that these very differences are an argument in favor of the desmoid reaction itself. If certain writers assert that the desmoid test is faulty because of the digestion of the catgut in the intestine, as, for example, Einhorn has done, without offering any experimental proof therefor, they underestimate the scientific ability of the author, for he has shown repeatedly, in preliminary experiments, that this is not the case. Since then the experiments have been repeated by his assistant, Wölfers, who has repeatedly inserted the sacs in the intestine during a gastro-enterostomy, and has found that the catgut was not attacked.[1] In achylia the desmoid reaction is without exception negative. The objection that lactic acid and pepsin may also act proteolytically is not altogether unfounded; it appears, however, to have more academic than practical interest. The author has not so far observed such a condition in the stomach, for the concentration of lactic acid, which would be necessary for so difficult a digestive process as that of dissolving catgut, must occur but seldom in the stomach. Furthermore, the author points out that he has never suggested that the desmoid reaction is a hydrochloric acid reaction, nor a substitute for a chemical examination of the gastric contents, but has advanced it as a test of the functional peptic activity of the stomach. The objection that in healthy individuals with good gastric digestion the test may be negative is not conclusive, for

[1] The author has made gastric examinations of apparently healthy individuals where the desmoid reaction was negative, and has found that there was either a latent anacidity, or, in spite of the presence of free hydrochloric acid, an extreme poverty in ferment, or a hypermotility of the stomach, whereby the pills were passed quickly through the stomach and were not digested. He also points out that if the undiluted gastric contents be examined for pepsin, by the method described on p. 473, without the addition of hydrochloric acid, it will be found that a gastric juice containing both free hydrochloric acid and pepsin will, in the undiluted state, be quite inactive, due to the fact that the acid is saturated with albumoses. It was through this important finding, which shows the insufficiency of the ordinary methods of examination by titration and pepsin estimation, that the author was led to take up the desmoid method, and he has widened his knowledge of the pathology and physiology of the stomach very materially by its means.

one may be dealing with hypermotility; and, as the author has observed a negative reaction with hearty eaters, he assumes that where the intake of food has been excessive, much of the food may pass through the stomach undigested, as an examination of the stools often reveals, despite the fact that the individual may feel perfectly well.[1] The desmoid reaction gives the situation exactly as it is in the stomach, not as one may conclude from observations made with the test-tube. The author believes that this fine power of distinction, which the desmoid test possesses, is the contribution which it has made to progress in gastric diagnosis.

The method is so well founded physiologically that one may question whether it is not suited as the basis for explaining certain clinical paradoxes which do not coincide with the ordinary views on gastric digestion. It seems to have a better basis than to trust to the absolute infallibility of the latter. In any event, it does seem to be a waste of time to discuss criticisms based on the assumption that the author has endeavored to replace the chemical examination of the gastric contents by the desmoid test, where, as a matter of fact, he has used them to supplement each other. Finally, he also wishes to point out that many of the tests have been made with sacs which have been faultily prepared, or have been made without reference to the author's original papers.

As the author has shown, the desmoid test does not, and should not always, give the same results as those obtained by an examination of the contents of the stomach, and he wishes to add that, according to Gentzen, if the test be made in the morning on a fasting stomach, the desmoid test is regularly positive.

Gentzen has given the pills in the morning to patients who have fasted since the night before, and has withheld food until the reaction appeared. He found that out of 53 normal cases 52 were positive in six to seven hours at the latest; it occasionally appeared after one to two hours. He concludes, as has Schreiber, from siphonage of the fasting stomach, that the organ in this condition contains a peptically active secretion. Whether this method of administration be of diagnostic interest for those who wish to make the desmoid test a test for free acid, with a constant coincidence of the presence of free acid and a positive desmoid test, and conversely an absence of acid and a negative test, cannot at this moment be said, for cases with absence of free hydrochloric acid have not so far been observed. As one will see, this method fails to give information regarding the digestive act after the administration of ordinary meals.

METHODS OF EXAMINING THE STOMACH WITH THE AID OF THE STOMACH-TUBE

INSTRUMENTS

Kussmaul was the first to employ the stomach-tube for the treatment, and von Leube the first to use it for the diagnosis of gastric affections. With its help we can at any time obtain the gastric contents for examination. We can also distend the stomach to any degree for diagnostic purposes. Unless there be a stenosis of the esophagus or at the cardia, rubber tubes which are quite soft and pliable are to be preferred. The surface of the tube must be smooth, the rubber soft but not too collapsible, the lumen large in relation to the entire diameter, and the opening at the lower end as large as possible. The smaller-sized tubes are generally easier to pass and less disagreeable to the patient, but become stopped up easily. In passing the smaller sizes we require the patient's help in swallowing, whereas the larger can be more readily pushed down the esophagus. No. 22 (Jack's patent),[2] with a diameter

[1] The author points out that the cases of negative desmoid reaction have become rarer since using sacs weighted with bismuth. These sink at once to the deepest lying portion of the organ, and allow the patient to assume a standing or sitting position, or, in case he is confined to bed, any recumbent position except that on the right side, so that the pills may not be carried by gravity into the duodenum.

[2] [I have found the Jack tubes very good, but a rather softer and more pliable tube will sometimes cause less gagging, especially upon the first introduction. We refer the reader to Hemmeter's Diseases of the Stomach, second ed., pp. 114–118, for additional details and hints upon the introduction of the tube.—Ed.]

of about 12 mm., is, the author believes, the most convenient size. They are provided with a lateral opening and a rounded closed end. See p. 445 in regard to the advantages of tubes with many perforations near the lower end instead of one lateral or terminal opening. The author devised the former for complete evacuation of the stomach, and in the Bern clinic they are used exclusively for this purpose. With the aid of a small glass tube for connection and a rubber tube about two feet long, the stomach-tube is connected to a large funnel, preferably of glass. [A funnel made of black vulcanite enables a better inspection of the material withdrawn. It is also less liable to break.—Ed.] These three pieces together constitute a siphon apparatus, by means of which we can easily empty and wash out the stomach. In certain cases a rubber bulb may be substituted for the connecting glass tube. This device permits the use either of pressure or suction. Varying manual compression of the tube takes the place of valves.

In inflating the stomach to determine its size we may employ either this bulb or a so-called stomach-pump. The latter is furnished with a two-way stop-cock, so that the barrel of the pump may be connected

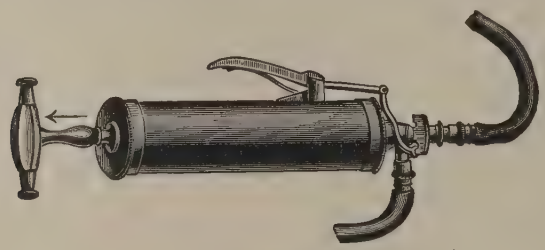


Fig. 204.—Stomach-pump.

with the stomach-tube or opened to the external air (Fig. 204). By means of a lever controlled by the hand holding the pump the stop-cock can be readily turned.

The stomach-pump formerly in common use for washing the stomach is entirely unnecessary and not to be recommended. No more forcible aspiration than that afforded by the siphon apparatus and bulb described above is desirable. Strong suction may easily detach bits of the gastric mucosa. For the same reason even the use of the bulb is not advisable for emptying the stomach. Moreover, it is usually unnecessary if the directions given on p. 442 be followed. The bulb is of greatest value in freeing the tube when the latter is clogged by solid particles of food. This should be done by forcing air through the tube rather than by aspirating.

TECHNIC OF INTRODUCING A SOFT STOMACH-TUBE[1]

The patient should be in the sitting posture, with his mouth wide open. The operator supports the patient's head with his left hand, and introduces the tube with his right without putting his fingers in the patient's mouth. The rounded end of the tube should be pushed back and down over the base of the tongue, exactly in the middle line. If there be no obstruction in the esophagus, we need not lubricate the tube with anything but water. If the patient can be persuaded to relax and breathe quietly and deeply, the tube can be quickly pushed into the

[1] See Examination of the Esophagus.

stomach. The patient need not attempt to swallow if we use the rather large tubes. It is important for the examiner to reassure him in every possible way, and to explain beforehand the steps of the process and its disagreeable features, so as to avoid frightening him during the ordeal itself. As soon as the tube has entered the esophagus but a few centimeters, the complete passage is readily effected. The distance from the teeth to the cardiac orifice in an adult is usually about 40 cm.

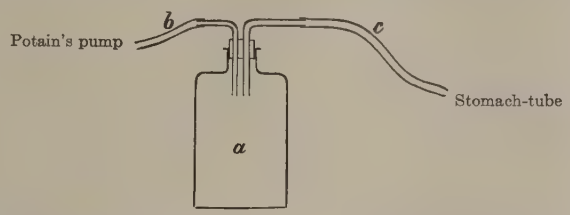


Fig. 205.—Arrangement of Potain's pump used as a stomach-pump: *a*, A wide-necked bottle fitted with a rubber stopper, through which are passed two glass tubes bent at right angles; *b*, tube leading to Potain's pump; *c*, tube connecting with the stomach-tube.

($15\frac{3}{4}$ in.). Continued deep breathing, even after the tube has been completely inserted, is very helpful to the patient.

Some patients exhibit so much dyspnea that an inexperienced examiner may think the tube is in the larynx or trachea, although the difficulty in breathing is due only to the psychic influence, perhaps to the pressure of the tube, or to obstruction from involuntary swallowing movements. Sometimes hissing respiratory sounds produce the impression that the patient is breathing through the tube (esophageal breathing). (Compare section on Examination of the Esophagus.) As a matter of fact, it is extremely difficult to introduce the tube into the larynx, especially if soft tubes be used, because the larynx closes the instant any foreign body touches its entrance, and because the epiglottis is depressed and the tube pushed into the esophagus by the voluntary or reflex swallowing act at the moment the tip of the tube gets into the pharynx.

If a fit of coughing occur as the tube is being introduced, it is well to withdraw it and try again. Any marked resistance, marked dyspnea, or much gagging upon the part of the patient usually means that the tube is caught in one of the fossæ pyriformes at the side of the larynx, and rolled up spirally over the entrance of the larynx. Then, if the examiner attempt to push it farther, the tube usually snaps back suddenly into the mouth. To avoid this difficulty we should endeavor to introduce the tube exactly in the median line.

In some very difficult cases it may be necessary to paint the pharynx with a 5 per cent. solution of cocain. (See section on Laryngoscopy and Tracheoscopy.)

INDICATIONS AND CONTRAINDICATIONS TO THE INTRODUCTION OF THE STOMACH-TUBE FOR DIAGNOSTIC PURPOSES

Indications.—Every slight gastric complaint does not indicate the employment of a stomach-tube, for it causes the patient too much discomfort; but its use is indicated where an absolute diagnosis seems impossible at the onset, or where the treatment employed has failed and the physician appreciates the necessity of revising the diagnosis by more exact methods.

Contraindications.—The stomach-tube is contraindicated in all grave disorders of respiration or circulation; in valvular lesions; in cardiac neuroses, etc., when the excitement accompanying the passing of the tube may in itself lead to danger, in aortic aneurysms (on account of

the danger of perforation); in patients liable to cerebral hemorrhage; and in those who have recently had hemorrhage from the lungs or the stomach.

THE VARIOUS STEPS IN THE EXAMINATION

The best time to introduce the tube is in the early morning, upon a fasting stomach, the patient having ingested, the previous evening, a rather abundant mixed meal.

We first cleanse the fasting stomach, extracting any residue or secretion which it may contain. After the tube has been introduced the patient, in the recumbent posture, is instructed to strain or cough gently, to aid in expelling any stomach-contents. If nothing appears, the attempt is repeated with the patient in the right or left lateral position. After the evacuation, or if nothing be obtained, we pour in at first a little lukewarm water, and later a pint at a time, and then empty the stomach again by depressing the funnel below the level of the stomach. If employing a funnel, the examiner must see that it is kept filled, so that the tube does not become empty, and hence stop the siphonage. In case any particles stop up the tube, it may be possible to force them back into the stomach by elevating the funnel again or by forcing air through with the bulb. Strong aspiration (holding the funnel very low, aspiration with the bulb or the stomach-pump) for the purpose of sucking the obstructing particles forcibly through the tube should be avoided, on account of the danger alluded to above. The stomach is washed out in this way until the returning fluid is clear. To avoid any interference with the test-meal given later, it is advisable to remove all the water. This can best be done by using the author's perforated tubes and the method described on p. 445 et seq. If any material was removed before beginning the washing, it should be saved for examination. (See p. 446.) If this was not possible, then whatever was obtained after the first dilution.

After emptying and cleansing the fasting stomach, the next procedure is to determine its size and position by distending it with air [1] or with water. This can be accomplished quite conveniently with the aid of the rubber bulb [or a Davidson syringe.—Ed.]. The patient should be in the dorsal decubitus, with the lower chest and abdomen exposed to view. We must inflate cautiously and stop whenever any pain is produced or too great tension results. After it is moderately distended inspection will generally disclose the size and shape of the organ. The latter do not, however, correspond to those of the normal stomach when it is filled with food. (See p. 424.) Nevertheless, dilatation may be diagnosed in this way. The position of the semilunar space and of the lesser curvature is of greater significance in this respect than that of the greater curvature, and in inspection of the inflated stomach one must observe the position of the lesser curvature as well as of the greater to avoid confusing a gastroptosis or loop-shaped stomach with one that is pathologically dilated.

The "hour-glass" stomach is very rare. It consists of two cavities connected by a constricted passage, and under certain conditions may be recognized by inspection of the inflated stomach.[2]

[1] This will be superfluous if we have already determined the measure accurately by inspection, by palpation, and by percussion. (See p. 424.)

[2] Virchow's Arch., 1895, vol. cxl, No. 3, p. 459, and Rosenfeld, Centralbl. f. inn. Med., 1903, No. 7.

When inspection alone fails to determine the shape and size of the stomach (*e. g.*, on account of abnormally thick walls), palpation and percussion of the inflated organ will usually determine the outline or, at least, the position of the greater curvature. Useful information concerning the capacity of the stomach may be obtained by measuring the amount of insufflated air which the patient can tolerate without discomfort. Luschka has estimated that a normal stomach will contain between $1\frac{1}{2}$ and 2 liters of gas; but these figures were determined upon cadavers, and are subject to considerable variations according to the character of the nutriment of different classes and countries. Hence these figures must not be applied to the living without reserve. Besides, some of the air may escape through the pylorus or upward through the esophagus. A large stomach is not necessarily diseased. An increase in size becomes pathologic only when it arises from stagnation of food following motor insufficiency. If continued insufflation produce a diffuse distention of the lower abdomen instead of a localized bulging in the epigastrium, we are justified in diagnosing an insufficiency of the pylorus (Ebstein).

When distending the stomach, we should note if any tumors be present, and also any changes in the position of the tumors. As soon as all these points have been determined, the air is allowed to escape, so as not to cause the patient any unnecessary discomfort. This is accomplished by pressing over the upper abdomen with the tube *in situ*. If this device does not promptly succeed, a slight change in the position of the tube will usually produce the desired effect. If not, the tube is probably obstructed and can be readily cleared by insufflating a little air. The tube with several perforations (see above) is of especial advantage here. Aspiration of the air is to be avoided. The tube should then be withdrawn, but not quickly enough to damage the mucosa of the cardia or esophagus by the edges of the orifices in the tube.

The fact that a patient's distention can be instantly relieved (p. 424) is one of the chief advantages of employing the tube instead of an effervescing powder. Röntgen-ray examinations have shown that the relations of a stomach inflated with air are not the same as when it is distended with food during digestion. Hence, in certain cases the size and shape of the stomach should be mapped out by inspection and percussion after filling it with lukewarm water (see p. 425), the patient being in the erect or sitting posture. If we fill the organ completely, in order to determine its entire outline after the manner of the radiograph (see p. 424), the tube should be employed so that the contents may be evacuated as soon as the patient experiences marked discomfort.

This method of gastric distention with air or water usually furnishes such accurate results in regard to the size and position of the stomach that it seems very questionable if "gastrodiaphany" can supplant it for practical purposes. The latter procedure consists in introducing a tube, with a small electric lamp at the tip, into the stomach, and thus transilluminating it. Röntgen-ray examination, however, after the stomach has been filled with bismuth paste, is valuable for the recognition of tumors which produce crenated shadows in the radiograph, and of an hour-glass stomach. The size and position of the stomach, also evident in the radiograph, are, however, determined with sufficient accuracy by the other procedures mentioned above. Tumors which cannot be appreciated by palpation will probably escape both these methods.

Inflation may be supplemented by palpation of the soft tube along the greater curvature of a relaxed stomach. Its tip can often be felt especially plainly, and the results of inflation thereby confirmed. Such palpation should be practised very cautiously.

TESTING THE GASTRIC FUNCTIONS BY MEANS OF A TEST-BREAKFAST

The principle involved follows: The patient takes a definitely determined meal upon a fasting stomach, *i. e.*, after the stomach has been emptied artificially or the first thing in the morning. We then draw conclusions as to the functions of the stomach from the amount and from the chemical character of the contents removed by the tube after the lapse of a certain time.

Various test-breakfasts have been advocated. For some purposes one kind is better; for others, another kind. If, for instance, we wish to test the behavior of a certain food in the stomach, then that food should be selected for a test-breakfast. Again, if we wish to determine the behavior of the stomach under an ordinary mixed meal, we select such a meal for our test, *e. g.*, Riegel's test-meal, which consists of a plate of mutton broth, a beefsteak (15 to 200 gm.), potato purée (50 gm.), and a roll. The test-meal should be given at the time the largest meal is usually eaten, for Marbaix[1] has shown that meals given at other times provoke an abnormal secretion from the mucosa. The Ewald-Boas test-breakfast is the most serviceable for general use. It is convenient and uniform. It consists of one roll (about 35 gm.), or the same amount of white bread, and two cups (400 cc.) of water or weak tea without milk or sugar. The patient should chew the bread very thoroughly. More useful and accurate information will be obtained from the "Sahli-Seiler's Butyrometric Test-breakfast." (See p. 479 et seq.) The test-meal is allowed to remain in the stomach a definite length of time until acted upon by the gastric secretion, and then withdrawn through the tube. Riegel's meal is ordinarily withdrawn at the end of four hours; the Ewald-Boas and the "butyrometric" at the end of an hour. If no contents can be obtained after the usual interval, the next day another meal should be ingested, and expressed after a shorter interval. Conversely, if information be desired in regard to the time the stomach requires to empty itself completely, the test may be repeated and the meal extracted after a longer interval.

The Ewald and Boas method of expression is the most convenient way of obtaining the stomach-contents. The patient is instructed to cough and strain down. The food is usually expelled better if the patient be in the right or left lateral, rather than in the sitting, posture. If the tube become clogged, we can generally free it by forcing a little air through, which is more convenient than diluting the contents by adding more water. When but little is expelled, it is advisable to employ pressure, so as to be sure that the stomach is empty, and thus to estimate correctly the amount of the meal which remained in the stomach. (See p. 482 in regard to the procedure for the "residue estimation.") If the method for completely emptying the stomach about to be described be employed, this procedure is entirely unnecessary.

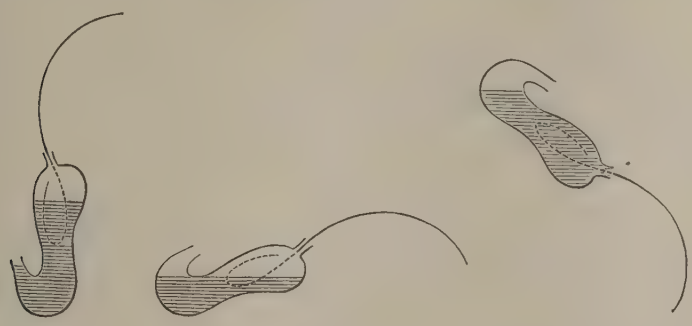
A PROCEDURE FOR THE COMPLETE EVACUATION OF THE STOMACH

The method of expression described above does not afford a guarantee that the stomach is completely evacuated. The subsequent lavage of the stomach gives, to a certain extent, an idea of the completeness, but does not afford quantitative results. The value of the so-called residue estimation has, with propriety, been questioned. As it is

[1] Marbaix, La Cellule.

of very great moment in investigations of the motility of the stomach, and the chemistry of that organ in general, that the stomach should be completely emptied, the author describes a process which he has used for several years in connection with his flour-soup method. This process can be used only when the contents of the stomach are completely fluid. The presence of even very fine solid particles may clog the tube and so prevent the complete evacuation of the organ. For this reason the author has used his flour soup in preference to the Riegel or Ewald test-meals. Further, one is never certain that the opening of the ordinary stomach-tube lies below the level of the contents. During the passage of the tube the lower end may curve upward, and project above the surface of the contents from the first, or after part of the contents have been expressed.

The author's procedure consists in the use of a stomach-tube of the ordinary caliber, but which, instead of a single opening, possesses a number of openings for the length of 30 cm. from the lower end. They



I
First posture.

II
Second posture.

III
Final posture, in which the total gastric contents escape through the tube.

Fig. 206.—Diagrammatic representation of the complete evacuation of the stomach by means of the author's sound with multiple openings. The figure is copied from the radiograph of a siphon-shaped stomach.

are of the same size as the opening at the end, and are placed more or less spirally. To empty the stomach, the tube is introduced until the greater part of the openings are apparently in the stomach. The contents of the stomach are now expressed in the usual way, with the patient lying on the left side. As soon as the flow has ceased, the examiner grasps the patient by the shoulders, shakes him well, and holds him over the left side of the bed or table, still retaining the left lateral posture, and depresses the head and trunk until the external end of the tube is lower than the cardia or the epigastrium. One of the openings of the tube near the cardia, which evidently is now the lowest point of the stomach, must be situated below the level of the contents of the stomach. The force of gravity or, if necessary, the aid of gentle pressure will thus empty the stomach completely. The schematic relations are shown in Fig. 206. It will be seen that the condition which interferes with the complete evacuation of the stomach by the ordinary method does not obtain here. With the many openings which the tube possesses, and the reversal of position of the patient, one of the

openings must lie at the deepest level of the fluid. The siphon-like form of the stomach must be taken into account. It might be that a quantity of the fluid could be trapped in the pyloric end of the organ, even when the cardia was the lowest point. For this reason the author recommends the patient to retain the left lateral posture, and in this position to bring the body over the edge of the bed. As the figures show, if this be done, even with a very marked tubular stomach, the pyloric end will be completely emptied of its contents. The author is completely convinced, by experiments which he has made in washing out the stomach after this procedure, that only the traces of contents which may adhere to the mucosa are left in the stomach. He regards this process as a very distinct advance in gastric technic. By it the objections which were raised to the butyrometric method, on the score of inability to empty the stomach completely, are removed. For therapeutic purposes, for lavage, and for cleansing the stomach before the administration of a test-meal, the procedure is of the greatest value. [Since adopting the author's method of expression I have invariably succeeded in recovering a sufficient amount of a test-meal for clinical examination, and venture to commend it heartily to the reader.—Ed.]

The stomach in the knee-chest posture may also be evacuated with the above-mentioned stomach-tube, but the position is not so convenient. If a tube with several openings be not available, one may place the patient in the same position, and gradually withdraw the tube, until the opening is at the cardiac orifice. Strauss' suggestion to replace the multiple opening tube by one with a single orifice should not be accepted.[1]

EXAMINATION OF THE CONTENTS OF A FASTING STOMACH

The materials removed from a fasting stomach are to be examined in the same way as the vomitus, so far as their microscopic and macroscopic peculiarities are concerned. For the chemical examination the same rules apply as for testing the expressed breakfast. (See p. 448 et seq.) If the fasting stomach contain remnants of the previous day's food, there must be a considerable degree of motor insufficiency, because a normal stomach would be empty within seven to eight hours, after even quite an abundant meal, and in any event should be empty in the morning.

Cranberry or Currant Test.—If we have not the opportunity to test the fasting stomach for determining motor insufficiency, nearly the same result can be accomplished, according to Ewald and Strauss, by giving the patient, at his evening meal, a tablespoonful of cranberry or currant preserve. We can decide upon a certain degree of motor insufficiency of the stomach if the expressed meal the next day contains any of the fruit or seeds. The advantage of the test is that it does not make any difference whether or not the patient has commenced upon his ordinary nourishment.

If we can obtain from the fasting stomach a considerable quantity of fluid containing free hydrochloric acid without any food-remnants, hypersecretion may be diagnosed, because, if empty, the stomach should secrete only a small amount of hydrochloric acid. The irritation of the tube or of the saliva swallowed may suffice to excite a mild secretion. Small amounts of fluid containing hydrochloric acid are not important, for Schreike has shown, and later Gentzen has proved, with the desmoid test, that the fasting stomach contains a small amount of secretion containing hydrochloric acid. Hence a small amount of such fluid is

[1] Zeit. klin. Med., vol. lxv, p. 162.

not sufficiently characteristic. The amount of acid fluid which can be withdrawn from a fasting stomach and still remain within the normal limits varies considerably, according to the individual authority. Ordinarily, not more than 10 cc. are found. Cases have been reported, however, where 20 to 50 cc. have been recovered without any noticeable disorder. Boas considers 100 cc. or over pathologic for a fasting stomach. Evidently there are no very sharp limits between a physiologic and a pathologic amount of secretion. To differentiate between primary hypersecretion and hypersecretion secondary to stagnation, compare p. 464, note 2. Normal gastric juice from a fasting stomach is thin, not at all slimy, with a specific gravity of only 1004 to 1005. It thus differs from gastric juice which contains the products of digestion, such as is obtained after a test-breakfast or when the food is retained. (Compare p. 448.)

If much lactic acid be present, we know that it is due to bacteriologic fermentation and, hence, it indicates a diminished production of hydrochloric acid, for normally the hydrochloric secretion of gastric juice inhibits lactic-acid fermentation.

Not infrequently a little yellowish or greenish bile-containing fluid, often alkaline, is expressed from the fasting stomach. It consists of duodenal juice, which entered the stomach from the gagging and vomiting while passing the tube. But if repeated examinations show that such fluid is always present, even if there have been no vomiting efforts, or, again, if it be constantly vomited in some chronic disease, there must be some stenosis of the duodenum below the ductus choledochus (Boas). This statement has recently been corroborated by various authors.[1] Gmelin's test will, of course, prove that the color is really due to bile. (See p. 575 et seq.) The reaction of the stomach-contents in such cases may be alkaline if the stomach no longer secretes enough acid to produce a neutral or acid reaction. If, on the other hand, the stomach secretes an abundance of hydrochloric acid and the fluid is stagnant for a considerable period, then the reaction may remain acid. In case the reaction is neutral or alkaline, we can prove that the fluid comes from the duodenum, because it will digest in an alkaline solution. For this purpose the fluid is placed, with a few fibrin flakes colored with Magdala-red, in an incubator, the reaction having been rendered, if necessary, distinctly alkaline by the addition of 1 per cent. soda solution. The fibrin flakes will be digested by the trypsin contained in the fluid, and the fluid will be colored red. If the fluid be of acid reaction, it is usually impossible to demonstrate the presence of trypsin, because in acid solutions trypsin is rapidly destroyed by the pepsin of the gastric juice.

For further methods of demonstrating the action of trypsin, and for recognizing intestinal juices in general, see later, in section on the Boas and Volhard-Boldireff methods for obtaining intestinal juice (p. 508 et seq.).

Gastric carcinomata which cannot be palpated may sometimes be diagnosed by washing out the empty stomach and finding macroscopic and microscopic constituents of the growth in the wash-water. The best method is to wash out the stomach thoroughly in the evening, and then to repeat the lavage the next morning without allowing the patient to take anything overnight. Sometimes a little undiluted fluid can be expressed through the tube for microscopic examination before the morning lavage. Characteristic bits or cells can thus often be obtained for examination, especially if the carcinoma be considerably ulcerated. The fluid should, of course, be centrifugated, and only the sediment examined microscopically. (See Solomon's test, p. 476 et seq.)

[1] Compare Herz, Ueber Duodenalstenosen, Deut. med. Woch., 1896, No. 23.

EXAMINATION OF THE GASTRIC FUNCTIONS BY MEANS OF THE ORDINARY (EWALD-BOAS) TEST-BREAKFAST

The expressed breakfast is, first of all, filtered. In what follows, the filtrate is called the "gastric juice."

APPEARANCE AND AMOUNT OF THE EXPRESSED MATERIAL; SPECIFIC GRAVITY OF THE GASTRIC JUICE; JUDGMENT OF THE GASTRIC MOTILITY

The conclusions to be drawn from the *appearance* of the test-breakfast in relation to the digesting function of the stomach are the same as were mentioned upon p. 427 et seq., with reference to the appearance of vomited gastric juice. (See especially the peculiarity of the particles of bread.)

The *amount* of the expelled material is of special diagnostic importance. The Ewald-Boas test-meal does not usually furnish physiologically more than 30 to 70 cc. of filtrate. But too much importance should not be given to these figures, because many variations occur and much larger amounts are within physiologic limits. A filtrate to the amount of 200 to 300 cc. makes motor insufficiency or hypersecretion probable. If there be a large volume of fluid and it is strongly acid from free hydrochloric acid, hypersecretion is very probable. Hypersecretion is, however, sometimes secondary to motor insufficiency, and is due to the continual stimulation of residual contents. If the expressed contents contain a large proportion of solid material, motor insufficiency is suggested. This diagnosis is confirmed if the fasting stomach contain particles of food. If the organ, eight hours after an ordinary meal, contain any remains of the meal, we have corroborative evidence of motor insufficiency. To determine the existence of true hypersecretion (independent of motor insufficiency), we should administer a roll with but very little or no fluid. Then if we can express a goodly amount of acid fluid, hypersecretion is definitely determined. Hypermotility may very properly be assumed if the volume of expressed material be decidedly diminished, but only when we have become convinced after lavage that the stomach is thoroughly emptied.

The specific gravity of the filtrate varies normally between 1012 and 1020. In hypersecretion and in sluggishness of the digestive mechanism it is diminished either by dilution or by deficient formation of soluble digestive products. Pure gastric juice without digestive products has (see p. 447) a specific gravity of only 1004 to 1005.

EXAMINATION OF STARCH DIGESTION

As is well known, the salivary enzyme changes starch first into soluble starch (amylum to amidulin or amylodextrin). Iodin colors the latter violet. The next change is to *erythrodextrin;* this gives a reddish to a mahogany-brown color with iodin. Finally, *achroödextrin* and *maltose* are formed (not, as was formerly believed, glucose). These last two products no longer produce characteristic colors.

In testing the gastric contents for the character of starch digestion, the point to determine is whether, besides starch, which always exists in considerable quantity, even in the upper portion of the intestines, there are also the above-mentioned terminal products of starch digestion. With a solution of iodin this can be easily accomplished. Achroödextrin produces no color, but it has a greater affinity for iodin than has

starch itself. Consequently, when slight traces of iodin are added to a uniform mixture of starch and achroödextrin, the iodin combines with the achroödextrin before it affects the starch. Therefore, if we add traces of iodin to a mixture of starch and achroödextrin, no color will result until an excess of iodin brings out the violet. A drop of a very dilute (wine yellow) Lugol's iodin solution [1] upon a glass rod is added to a small portion of the residue on the filter-paper, or even to the filtrate (because the latter always contains soluble starch). If achroödextrin be present, no color will appear until an excess of iodin is added. If, on the other hand, no starch digestion has occurred, the slightest trace of iodin will produce a violet color.

If a large volume of gastric contents be at our disposal, the test may be performed as follows: Lugol's solution (0.1 gm. iodin, 0.2 gm. potassium iodid, 200 cc. water) or centinormal iodin solution is added drop by drop to the filtrate. The amount added before a violet color appears will furnish an approximately accurate quantitative measure of the degree of starch digestion. The latter, of course, depends not only upon the rapidity of enzyme action, but also upon the degree of the absorption of the product formed.

Starch digestion is a function of the salivary enzyme. Its action is apparent partly in the mouth and partly in the stomach for a short time after the meal. Hence, starch digestion would naturally seem of little importance in the diagnosis of stomach diseases. But this is not really so, because an increased acidity will interrupt starch digestion very quickly. A blue color is obtained on the addition of the smallest quantity of iodin solution. On the contrary, with hypoacidity starch digestion progresses very favorably and completely. Hence, the degree of starch digestion serves as a rough test of the hydrochloric acid secretion. Boas claims that a digestive fluid containing 0.15 per cent. hydrochloric acid will arrest starch digestion. Nevertheless, even with normal gastric digestion, achroödextrin is present in the Ewald breakfast one hour after its ingestion. It was probably produced before enough acid had been secreted to reach the above degree of concentration. Achroödextrin is often absent in hyperacidity. Lactic acid does not impede starch digestion until it is more concentrated than hydrochloric acid, so that starches are frequently well digested in the gastric contents in hypomotility (Stauungsmagen) in case the stomach contains lactic, instead of free hydrochloric, acid.

QUALITATIVE EXAMINATION OF THE FILTERED GASTRIC JUICE FOR ACIDS

The reaction of the filtered gastric juice is, first of all, tested with litmus-paper. If the reaction be acid (as is almost universally the case), we get no information about the presence of hydrochloric acid, and especially of free acid, in the gastric juice, since besides acids, salts, particularly the acid phosphates, also turn blue litmus red.

To determine whether the acid reaction is due to free acid or only to acid salt we employ Congo-red, in the form of commercial Congo-red paper. If the gastric juice turn a strip of this paper blue, some free acid must be present: either free hydrochloric or some organic acid.[2]

[1] A few drops of tincture of iodin added to a 1 per cent. solution of potassic iodid.

[2] Congo-red is not at all changed by acids combined with proteins or with organic bases, and by acid phosphates only in such concentrations as do not occur in the stomach. The reaction may be regarded in the case of stomach-contents as one for free hydrochloric acid.

To decide whether the acid is organic or free hydrochloric we employ various qualitative tests.

Tests for Free Hydrochloric Acid.—The presence of free hydrochloric acid in the gastric contents shows that a sufficient quantity of hydrochloric acid has been secreted to combine with the basic contents of the stomach, especially the proteins of the food, so that an excess of acid remains. Concerning the clinical significance of the presence of free hydrochloric acid, see p. 461.

The reactions with methyl-violet, tropæolin 00, and dimethylamidoazobenzene have not proved satisfactory clinically. The following tests are the best for the purpose:

Congo-red Reaction.—Congo-red, in the form of the paper impregnated with the dye, is changed by other acids than hydrochloric acid, but only in such concentrations as occur but infrequently in the stomach. In any case the change in color is never so dark blue as with hydrochloric acid, so that a dark-blue reaction may be set down to the presence of the latter.

Phloroglucin-vanillin Reaction (Gunzburg's Reagent).—The reagent consists of phloroglucin 2 gm., vanillin 1 gm., alcohol 30 gm. One or two drops of this solution are placed in a porcelain dish and mixed with the same amount of gastric juice. The dish is then gently warmed over a small flame. If free hydrochloric acid be present, the drying margins of the mixture will develop a beautiful carmin-red color. If absent, the solution dries up, leaving a brown or yellow color. The reaction becomes a little more sensitive in doubtful cases if we employ rather more gastric juice than reagent.

The phloroglucin-vanillin test gives a positive reaction in the presence of 0.005 per cent. hydrochloric acid.

Tests for Lactic Acid.—*Uffelmann's reagent* is commonly employed to test the gastric juice for free lactic acid. It consists of a mixture of 20 cc. of a 1 per cent. carbolic acid solution, with 1 drop of dilute ferric chlorid. This solution is diluted until the color becomes a transparent amethyst blue. The reagent should be freshly prepared before each test, since the violet color disappears after a short time. This is a very delicate reagent: even traces of lactic acid change it to a beautiful canary yellow or greenish yellow. Mere decoloration without the formation of any pronounced yellow shade does not suggest lactic acid, because proteids, salts, and hydrochloric acid might produce such a result. Uffelmann's reaction may also be performed by adding to the fluid to be tested one or two drops of a very weak (5 per cent.) solution of ferric chlorid (without carbolic acid). If the fluid contains lactic acid, it will become distinctly yellow to green. In a doubtful case the same amount of ferric chlorid should be added to water for comparison. Uffelmann's reaction is not quite reliable, because certain sugars, peptones, alcohol, tartaric, citric, malic, racemic, and oxalic acids and various other substances produce a similar color. Another objection is that the reaction may be prevented by the presence of phosphates and a considerable excess of hydrochloric acid. The yellowish tint of the stomach-contents, and sometimes the turbidity due to the addition of the ferric chlorid, may also affect the reaction. Greater accuracy will result if we isolate the lactic acid by extracting the gastric juice with ether, removing the ether by evaporation, and then perform the test upon the ether residue dissolved in water. Uffelmann's test has

been very appropriately modified by H. Strauss.[1] By this method all sources of error are avoided and a quantitative result obtained.

Strauss' Method of Determining Lactic Acid.—He extracts the gastric contents with ether, but does not evaporate the ether. He shakes the ethereal extract with a dilute solution of ferric chlorid, according to Fleischer's method. If the watery layer shows a greenish coloration, the reaction is positive. By employing definite quantities of reagent and solution the intensity of the coloration can be made to furnish an approximate estimate of the amount of lactic acid. The procedure is as follows: 5 cc. of gastric juice are put into a separatory funnel (Fig. 207) having two division marks, one corresponding to a volume of 5 cc. the other to that of 25 cc.; ether is now added to the 25 cc. mark. The solutions are then shaken vigorously. After the mixture has settled into layers the gastric juice at the bottom is drawn off by means of the stop-cock. Distilled water is then added up to the 25 cc. mark. Then 2 drops of a dilute solution of ferric chlorid (containing 1 part ferric chlorid to 9 parts of distilled water) are added, and the mixture again vigorously shaken. If more than 1 per 1000 of lactic acid be present, the layer of water below is colored an intense greenish yellow. Smaller amounts do not produce any distinct color change. Strauss' method eliminates all the sources of error of the ordinary Uffelmann's reaction (above mentioned). None of the substances which produce a similar reaction (peptones and carbohydrates), nor substances which mask the reaction (hydrochloric acid and phosphates) will be taken up by the ether in any appreciable quantities. The ether employed should be free from alcohol. This method suffices for all practical purposes. It should be remembered that Strauss' test may be negative if the lactic acid present be completely combined with the proteins of the gastric juice. The acid albuminate of lactic acid does not then give up lactic acid to the ether. In such a case, which can occur only when the gastric juice does not react for free acids, it is advisable to repeat the shaking after hydrochloric acid has been added to the gastric juice up to a beginning of the Congo-red reaction.

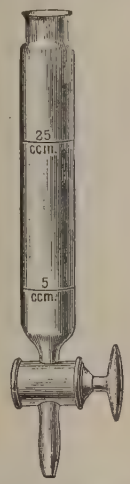


Fig. 207.—Separatory funnel.

Martius' experiments (see p. 462 et seq.), contrary to the old idea, prove that the formation of lactic acid is not a part of normal gastric digestion, but is rather due to bacterial fermentations, which are normally prevented by the presence of the hydrochloric acid of the gastric juice. The occurrence of lactic acid in the expressed meals, as demonstrated by Strauss' method, must, therefore, be considered a pathologic phenomenon. This points both to a stagnation of the gastric contents and to the absence or diminution in the amount of the free hydrochloric acid, for only when these factors occur together is opportunity furnished for abundant lactic-acid fermentation. Hence a large quantity of lactic acid is found with *motor insufficiency of the stomach*, more particularly from a stenosis of the pylorus, and then only when associated with diminished hydrochloric-acid production. As experience shows, this is generally due to carcinoma of the pylorus; hence a certain amount of significance has justly been attached to the demonstration of lactic acid in the stomach-contents as suggesting the diagnosis of carcinoma of the stomach. But the opinion, originally advanced by Boas, that the presence of lactic acid in the gastric juice was pathognomonic of this lesion, has not been confirmed. *Benign stenosis and gastric insufficiencies*, when combined with deficient secretion of hydrochloric acid, have repeatedly furnished a positive test to lactic acid.

[1] Berlin. klin. Woch., 1895, No. 37.

One objection to all the lactic-acid tests which demonstrate lactic-acid fermentation in the stomach is that ordinary food, and in particular Ewald's test-breakfast, always contains preformed lactic acid. Boas, for this reason, substituted a thin oatmeal porridge for the ordinary test-meal, there being no lactic acid in oatmeal. However, this precaution seems really unnecessary, considering the slight amount of preformed lactic acid which is contained in the ordinary test-breakfast, if diagnostic importance should be attached only to a very pronounced lactic-acid reaction. The advantage of Strauss' method is that while it estimates fairly accurately the amount of lactic acid, it is not sufficiently sensitive to give a positive reaction from the lactic acid in an ordinary roll made with water (not milk), without lactic-acid fermentation in the stomach.

Detection of Volatile Fatty Acids.—If the volatile fatty acids—*butyric*, *acetic*, or *valerianic*—be present to any extent, they are easily recognized by their characteristic odor. More accurate tests are too complicated and hardly practical. Traces of butyric acid occur normally after the ingestion of foods containing butter. Its presence is to be attributed to the action of the fat-splitting ferment of the gastric juice, recently more exactly studied by Volhard. The two other volatile fatty acids, like lactic acid, arise only as the result of fermentation and stagnation of the gastric contents, although traces do, of course, occur from what is contained in the various food-stuffs.

QUANTITATIVE TESTS FOR ACIDS

The quantitative analysis of the gastric juice is peculiarly difficult, because organic acids, and especially acid salts, may be present as well as hydrochloric acid, and because we must also differentiate between free hydrochloric acid and that which is combined loosely with the proteins, as we have already explained in connection with the qualitative hydrochloric-acid tests. To make clear the complexity of the condition, we may arrange in the following table the acid-reacting components of the gastric juice, *i. e.*, those turning blue litmus-paper red, in one group, and the chlorin-containing constituents, which we must consider in testing for hydrochloric acid, in another:

1. Acid-reacting constituents of the gastric juice.
   (*a*) Free and combined with proteins, hydrochloric acid.
   (*b*) Organic acids.
   (*c*) Acid salts (acid phosphates).
2. Chlorin-containing constituents of the gastric juice.
   (*d*) Free hydrochloric acid (producing color reactions).
   (*e*) Hydrochloric acid which is loosely combined with proteins produces no color reaction, but reacts acid to litmus and phenolphthalein. (This is usually called combined hydrochloric acid.)
   (*f*) Chlorids, neither reacting acid nor producing any color reaction.

Titration of the Total Acidity of the Gastric Juice.—In order to determine the total acidity, we first of all titrate the gastric juice with a $\frac{N}{10}$ sodium hydroxid solution, *i. e.*, we determine the number of cubic centimeters of the sodium hydroxid solution necessary to neutralize a definite volume of gastric contents. The technic is as follows: As is well known, a normal sodium hydroxid solution is one which contains in each liter as many grams of the substance in question as its molecular weight. A decinormal $\left(\frac{N}{10}\right)$ solution is made from

this by diluting it 10 times. According to the definition, equal volumes of normal solutions neutralize each other: 1 cc. of a $\frac{N}{10}$ NaOH solution neutralizes exactly 0.1 cc. of a normal HCl, etc.

THE PREPARATION OF ACIDIMETRIC NORMAL SOLUTIONS

While formerly it was the custom to use oxalic acid as a standard substance for the preparation of a standard acid, by dissolving 63 gm. of the non-effloresced acid in water, and making up to one liter, more recently, owing to the somewhat inconstant composition of the crystals, pure sodium carbonate (dry) has been used for the purpose of preparing a normal solution. From this a standard decinormal solution of hydrochloric acid is prepared.

Normal Hydrochloric Acid (1000 cc. = 36.458 gm. HCl).—Pure concentrated hydrochloric acid is diluted with water to about 1020 specific gravity, and the resulting solution is titrated against a solution of sodium carbonate. For this purpose 5 gm. of pure sodium bicarbonate are heated in a platinum crucible over a flame for one hour. The heat must be applied gently. The heating is continued until the platinum crucible and its contents no longer lose weight. It is then allowed to stand in a desiccator and finally weighed. From this one weighs out exactly 2 gm., dissolves in 100 cc. water, adds three drops of methyl-orange solution (0.2 in 1000), and titrates with hydrochloric acid until the yellow color of the solution changes to orange. The hydrochloric acid is then diluted with water until 37.7 cc. of the acid are required to neutralize 2 gm. of the sodium carbonate.

Normal Sodium Hydroxid (1000 cc. = 40.058 gm. NaOH).—Fifty gm. of sodium hydroxid are dissolved in cold distilled water, and diluted up to 1000 cc. This solution is titrated against the normal hydrochloric acid, using methyl orange as an indicator, and further diluted until 1 cc. of the alkali exactly neutralizes 1 cc. of the acid.

A decinormal solution is prepared by diluting the normal solution 1 : 10; a centinormal solution, by diluting 1 : 100.

THE TITRATION OF THE GASTRIC CONTENTS

A buret is filled to the zero-point with decinormal sodium hydroxid solution. In a porcelain dish or in a beaker, held over a white sheet of paper, 10 cc. of the filtered gastric juice to be investigated is placed.[1] A few drops [two] of an alcoholic solution [1 per cent.] of phenolphthalein are added. The decinormal solution of sodium hydroxid is allowed to run in slowly until the red color is permanent [and until no deepening of the tint is caused by addition of the alkalis.—Ed.]. The amount of decinormal solution used for neutralization is the expression of the acidity of the gastric contents. The acidity may be expressed in two ways: It may be calculated in terms of a single acid, or, as Jaworski has suggested and a number of writers have followed, in degrees of acidity. Usually the acidity is calculated in terms of free hydrochloric acid. In order to do this it is only necessary to remember that, according to the definition of normal solutions, equal volumes of these neutralize one another: 1 cc. of normal sodium hydroxid therefore neutralizes 1 cc. of normal hydrochloric acid. Normal hydrochloric acid contains in 1 liter one equivalent (*i. e.*, 36.5 gm.) hydrochloric acid; 1 cc. normal hydrochloric acid contains, therefore, 0.0365 gm. hydrochloric acid. This amount of hydrochloric acid corresponds to 1 cc. of normal sodium hydroxid. One cc. of the decinormal sodium hydroxid used corresponds to 0.00365 gm. hydrochloric acid. From these data the calculation of the degree of acidity

[1] Martius has shown that in the quantitative determination of the gastric contents the unfiltered juice should be used, because the acid is divided unequally between the solids and liquids, the solids holding back the greater part of the acid. For practical purposes, however, it is easier to perform the test with the filtered contents. In using the butyrometric method, the filtrate must be used.

in terms of hydrochloric acid is quite simple. If one has used 5 cc. of decinormal sodium hydroxid to neutralize 10 cc. of the gastric juice, this corresponds to an amount of hydrochloric acid in the 10 cc. of gastric contents of $5 \times 0.00365 = 0.01825$ gm. of hydrochloric acid. Calculated in per cent., *i. e.*, the amount in 100 cc. = 0.1825 per cent. This method of calculating the amount of hydrochloric acid does not, indeed, give us the true amount of hydrochloric acid, for other factors in the gastric juice influence the results, but it has the advantage that it gives us an idea of the amount of hydrochloric acid which the gastric juice in question can contain. The calculation of the acidity in terms of "degrees of acidity" is done by reckoning the number of centimeters of decinormal sodium hydroxid which are required to neutralize 100 cc. of gastric juice. In order to do this one has only to multiply the number of centimeters of decinormal alkali used by 10. A gastric juice which requires 5 cc. of decinormal sodium hydroxid has, therefore, a degree of acidity of 50. This method of calculation has the advantage that it expresses exactly what it means, while the calculation to hydrochloric acid is based on the erroneous supposition that the whole of the acidity is due to hydrochloric acid. On the other hand, the calculation to hydrochloric acid gives us a clearer picture of the conditions in the gastric juice.

Strictly in all titrations of the acidity of the gastric contents one should make use of the facts which Moritz has brought out in his work on the acidity of the urine. This has, however, not been done in clinical investigations. Besides his work, one must take into account the investigation of Volhard on the influence of the protein and albumose content of the gastric juice in respect of their power to combine with alkalis. Volhard has found that considerable quantities of alkali, which we assume in the above method to be used in neutralizing acid, are in reality taken up by the proteins present in the gastric juice, for the proteins combine with alkalis as well as with acids. As phenolphthalein is a relatively insensitive indicator for alkali, the end-reaction only takes place when not merely the alkali affinities of the acid, but also of the proteins, are saturated. As a result, the usual values for acidity which have hitherto been given are too high. This may to some extent explain the differences which have been observed between the clinical presence of hyperacidity and the amount of acid as found by titration. In some instances evidences of hyperacidity have been found where the titration values have been low, while, on the other hand, high values have been found by titration where the patient has suffered no inconvenience. In order to avoid this difficulty Volhard suggests the use of litmus by the drop method (taking out a small amount of the gastric juice with a glass rod, and applying it to blue litmus), or the use of alizarin red, indicators of the second group, of moderate sensitiveness to acids, which react alkaline with the compounds of alkali with proteins.

Quantitative Estimation of the Hydrochloric Acid and Chlorids in the Gastric Juice.—The estimation of the total acidity of the gastric juice is a very simple chemical procedure, but the determination of the amount of hydrochloric acid contained in the gastric juice appears more difficult, because we have to consider separately the factors *d*, *e*, and *f* (p. 452). A chlorin estimate alone is of no value in judging the amount of hydrochloric acid, for it would give only the total sum of $d + e + f$, and include chlorids of the food as well. What we wish to determine is the sum of $d + e$ (*i. e.*, the amount of hydrochloric acid secreted by the stomach, both free and combined.

Estimation of the Total Hydrochloric Acid of the Gastric Juice ($d + e$, p. 452).—*Sjöqvist's Method.*—This depends upon the fact that the acids which are absolutely free, as well as those which are but loosely combined with proteins, are changed to their corresponding barium salts if mixed with barium carbonate. If the

mixture be then evaporated to dryness and incinerated, the barium salts of the organic acids will be retransformed to barium carbonate, but the hydrochloric acid will remain fixed as barium chlorid. This can then be isolated from the ash by extraction with water, and then titrated with a solution of potassium bichromate, and the amount of hydrochloric acid be calculated from this. The preformed chlorids in the stomach do not influence the titration, since the latter is concerned only with the barium and not with the chlorid salts.

The steps of Sjöqvist's method are as follows: 10 cc. of gastric juice are slowly evaporated to dryness in a silver platinum dish, with an excess of barium carbonate (free from chlorin). The residue is then kept at a red heat for a few minutes. After cooling, the residue is first digested with 10 cc. of water, and then extracted repeatedly with hot water until the filtered extract amounts to 50 cc.

In order to titrate for barium we add to the solution one-fourth to one-third its volume of alcohol, and 3 to 4 cc. of a solution of 10 gm. of acetic acid and 10 gm. of sodium acetate in 100 cc. of water. These additions facilitate the separation of the barium chromate and prevent the precipitation of calcium chromate from any calcium salt that may be present. An 8.5 per cent. solution of chemically pure potassium bichromate is added from a buret to the solution until the barium is completely precipitated. So-called "tetra paper" (tetra-methyl-paraphenylene-diamin paper) will serve to indicate the end of the reaction. Any excess of potassium bichromate will produce a blue color. Every cubic centimeter of bichromate solution which it was neeessary to add in order to complete the end-reaction corresponds to 4.05 mg. of hydrochloric acid. Since this reaction is not sharply defined, Sjöqvist has recently improved his method at the expense of simplicity by changing the final titration with bichromate to a much more sharply defined iodin titration. Iodin is quantitatively liberated by adding KI and HCl to the bichromate, and the iodin is determined in the well-known way by titrating with sodium thiosulphate and starch. (See Lehmann's sugar titration, p. 621.) For the technic of this modification we must refer to the original communication in Vol. V of the Scandinavian Archives of Physiology, 1895.

Leo's Method.—Leo's method is based on the fact that both free and combined hydrochloric acid are neutralized by calcium carbonate, while acid phosphates and other combinations reacting in the titration with sodium hydroxid show the same acidity after treating with calcium carbonate as before.

Leo first removes the volatile fatty acids by distillation, and the non-volatile fatty acids and the lactic acid by extraction with ether, and then estimates the total acidity of the specimen of gastric juice. In another portion he combines with calcium carbonate both the free hydrochloric acid and that combined with the proteins, and then titrates again. The amount of the acidity which disappears after the addition of calcium carbonate corresponds to the hydrochloric acid present. Calcium chlorid, formed in the neutralization of the hydrochloric acid, necessitates (on account of the probable presence of acid phosphates) especially skilful manipulation when performing the test. If calcium chlorid be absent, the titration of the acid phosphates will be represented by the following formula: $PO_4H_2K + NaOH = PO_4HKNa + H_2O$. But if calcium chlorid be present in the solution at the same time, the following formula will represent the titration: $2PO_4H_2K + 4NaOH + 3CaCl_2 = (PO_3)'Ca_3 + 2KCl + 4NaCl + 4H_2O$. In the latter case we need double the quantity of sodium hydroxid for neutralization. Leo adds an excess of calcium chlorid to both specimens before titration, in order to exclude the influence of the calcium chlorid formed by the neutralization with calcium carbonate, when comparing the two titrations. For the details of the technic consult Leo's own communication.[1]

Leo's method will also serve the purpose of estimating at the same time the quantity of acid phosphates. It must be pointed out that the principle of Leo's method has been condemned by F. A. Hoffman[2] and others.

Lütke-Martius' Method.—Lütke-Martius' is one of the simplest methods for the determination of the total amount of hydrochloric acid secreted (free HCl + that combined with proteins).

We first estimate the total amount of chlorin in a specimen of gastric contents[3] (see below). This is represented by *a*. Another specimen of the gastric contents is incinerated, the chlorin in the ash estimated, and represented by *b*. The

[1] Diagnostik der Erkrankungen der Verdauungsorgane, Berlin, 1890.

[2] Centralbl. f. klin. Med., 1890, vol. xl.

[3] Martius employs the unfiltered gastric contents exclusively, instead of the filtrate. (See note p. 453.)

latter then represents the chlorin of the chlorids, because the HCl is volatile By subtracting *b*, the chlorin of the chlorids, from *a*, the total chlorin, we get $a - b$, the chlorin of the hydrochloric acid secretion.[1]

Volhard's method estimates the total amount of chlorin. An excess of strongly acid silver-nitrate solution is added to a measured quantity of the gastric contents, so that all the chlorin present will be combined with the silver. We can then determine whatever excess of silver remains uncombined in the filtrate by titration with ammonium thiocyanate. The silver will be precipitated as insoluble silver thiocyanate. Iron alum or sulphate will serve as an indicator to show when the precipitation is complete. It may be added to the silver solution at the beginning. In adding the ammonium thiocyanate, the red color of the ferric thiocyanate will persist only after all the silver has been completely precipitated as silver thiocyanate. The details of the technic are contained in the following quotation from Lütke:

The following normal solutions are essential:

1. $\frac{N}{10}$ silver solution containing 17 gm. of silver nitrate in a liter: Ferric sulphate is also added to the solution as an indicator, and an excess of nitric acid. The method of preparation is as follows: 17.5 gm. of silver nitrate are dissolved in about 900 cc. of 25 per cent. nitric acid, and 50 cc. of liquor ferri sulphurici oxydati are added to the solution and the volume made up to 1 liter. The solution is standardized with a $\frac{N}{10}$ HCl solution in the usual way.

2. $\frac{N}{10}$ ammonium thiocyanate solution: 7.6 gm. of $CNSNH_4$ in a liter. About 8 gm. of ammonium thiocyanate are dissolved in 1 liter of water, and the absolute quantity contained in this solution estimated by means of the $\frac{N}{10}$ silver solution. For this purpose 10 cc. of the (iron-containing) silver solution are placed in a beaker, and 150 to 200 cc. of water added; then the thiocyanate solution is allowed to flow in from a buret until a faint reddish color appears and persists, *e. g.*, if 9.7 cc. had been used for this purpose, then 970 cc. of the thiocyanate solution should be diluted up to 1000 cc. After such a dilution a further trial is made to determine accurately that it is a $\frac{N}{10}$ solution.

(*a*) *Estimation of the Total Chlorin.*—Ten cc. of the stomach contents, well mixed, are placed in a 100 cc. graduated flask. The graduate in which the 10 cc. are measured must previously be rinsed out twice with water. Then 20 cc. of $\frac{N}{10}$ silver solution are added; the mixture is well shaken and allowed to stand ten minutes. If there be a marked color to the stomach-contents, we may decolorize by adding 5 to 10 drops of a potassium permanganate solution (1 in 15). This is not often necessary. The permanganate solution should not be added until all the chlorin is already combined with the silver, otherwise the permanganate will split up the hydrochloric acid and form free chlorin, which volatilizes, so the result of the analysis would be questionable. After decolorization has taken place we add water up to 100 cc., shake well, and filter through a dry filter-paper into a dry beaker.

Fifty cubic centimeters of this filtrate placed in a beaker are now titrated with the $\frac{N}{10}$ thiocyanate solution.

The total amount of chlorin is calculated as follows: The number of cubic centimeters of thiocyanate solution required is multiplied by 2, and the product deducted from the volume of the silver solution used (20 cc.).

(*b*) *Determination of the Chlorids.*—Ten cc. of well-mixed gastric contents in a platinum dish are evaporated to dryness over a water-bath. This may also be done by heating the dish with an alcohol or gas burner, using an asbestos plate instead of a water-bath. Evaporation proceeds quickly, and no loss takes place from sputtering. The residue is incinerated over the direct flame so long as the ash burns with a bright, luminous flame. Excessive and prolonged heating is superfluous and to be avoided, because the chlorids volatilize at red heat. After the burning of the residue the moistened ash is pulverized with a glass rod and extracted with about 100 cc. of warm water, and the fluid then thrown upon a filter. Experience has shown that this amount of water is sufficient for a complete extraction of the ash. If it be doubtful, however, whether all the chlorin has been washed out, a few drops of the silver solution may be added to the last few drops of the filtrate. Any cloudiness would indicate the presence of chlorin and necessitate further extraction. The entire filtrate is then placed in a beaker with 10 cc. of $\frac{N}{10}$ silver solution, and titrated with

[1] See following pages. For a correction of this method see Reissner, Zeit. f. klin. Med., vol. xliv, p. 75.

the $\frac{N}{10}$ thiocyanate solution. The amount of chlorin held in combination is calculated by subtracting the number of cubic centimeters of the thiocyanate solution from the amount of silver used (10 cc.).

(*c*) *Determination of the Hydrochloric Acid.*—The amount of hydrochloric acid contained in 10 cc. of gastric contents is calculated from the two values found (total chlorin (*a*) and chlorin of the chlorids (*b*)) by subtraction. From the amount of total chlorin expressed in cubic centimeters of $\frac{N}{10}$ solution, the amount of chlorin of the chlorids, expressed in the same way, is deducted. By multiplying the result by 0.0365, the absolute amount of hydrochloric acid contained in 100 cc. of stomach-contents, or the percentage of the hydrochloric acid, is obtained.

The author's own experience shows that the amount of $\frac{N}{10}$ silver solution employed in both determinations (a = 20 cc., b = 10 cc.) has been found quite sufficient to combine with all the chlorin. If it should happen that a gastric contents be observed with a greater content of chlorin, then more of the $\frac{N}{10}$ silver nitrate solution must be added.

O. Reissner[1] has called attention to the fact that the hydrochloric acid values obtained by means of the Lütke-Martius method are erroneous in one respect, since the gastric juice contains ammonium chlorid, the ammonia of which, as shown by Sticker, is obtained chiefly from the saliva, although under pathologic conditions it may also arise within the stomach, from the putrefaction of albumin. When the residue of the gastric contents is incinerated in the Lütke-Martius method to remove the hydrochloric acid and to obtain the value b (see p. 455), the ammonium chlorid is volatilized as well. The value b for the chlorin of the chlorids is consequently too low, and the value $a - b$ for the secreted acid will be correspondingly too high. This explains the fact that the Lütke-Martius method sometimes gives a value for the secreted hydrochloric acid which is greater than the total acidity, a condition of affairs which is manifestly impossible, since the total acidity includes not only the hydrochloric acid, but the acid phosphates as well. Reissner has also shown how to avoid this source of error. He eliminates the ammonium chlorid before determining the value of a; the subtraction $a - b$ will then give a correct result. Instead of determining a directly by titrating the gastric contents with the silver and thiocyanate solutions, Reissner advises neutralization of a measured quantity of the gastric contents, its incineration in a platinum dish, the solution of the ash in hot water, and the titration of the filtrate in the customary manner. By this modification the ammonium chlorid is volatilized and eliminated from the chlorin value a. In the neutralization Reissner believes it is best not to go beyond the neutral reaction upon litmus, since, when phenolphthalein is employed as an indicator, the end-reaction is postponed, and there is danger that the chlorin of the ammonium chlorid will be partly fixed by the sodium as sodium chlorid.

Hehner-Maly's Method.—Hehner-Maly's method (recommended by von Leube for clinical work) is based on the fact that where a mixture of organic and inorganic acids is neutralized and reduced to an ash, the organic salts are changed to alkaline carbonates by the process of combustion, but the inorganic salts remain neutral. If this alkalinity, *i. e.*, an equivalent acidity, be deducted from the total acidity, the remainder is the acidity due to mineral acid.

For the gastric juice the process is as follows: 10 cc. of gastric juice are titrated in the usual way with $\frac{N}{10}$ NaOH, and with phenolphthalein as an indicator. The neutralized solution is evaporated to dryness in a platinum dish and then incinerated, the ash dissolved in distilled water, and the alkaline solution titrated with $\frac{N}{10}$ acid (oxalic acid or hydrochloric acid, with phenolphthalein again added as an indicator) until the decoloration is complete. The $\frac{N}{10}$ acid used in the titration corresponds to the acidity caused by organic acids. To determine the amount of hydrochloric acid, this value is simply to be deducted from the total acidity. This method is very simple and well adapted for clinical purposes. The only disadvantage is that the acid phosphates are estimated as HCl, for they act as mineral acids when reduced to ash. Very accurate results can be obtained by estimating the acid phosphates according to Leo's method (p. 455), and deducting the acidity belonging to them from the HCl as obtained by Hehner-Maly's method. Of course, the hydrochloric acid would be determined at the same time by Leo's method, so that Hehner-Maly's method would be needed only for the determination of the organic acids.

[1] Zeit. f. klin. Med., vol. xlviii, parts 1 and 2, p. 106.

This method, however, gives incorrect results in respect to organic acids in case these include the higher fatty acids, which are insoluble in water, and consequently not completely neutralized by the addition of $\frac{N}{10}$ NaOH. Should it be desired to estimate these higher fatty acids, the gastric contents, neutralized by means of the $\frac{N}{10}$ NaOH, must be well shaken with a generous quantity of ether, and any acidity arising from these fatty acids neutralized by the addition of an alcoholic $\frac{N}{10}$ NaOH. This neutralized ethereal solution is then added to the neutralized watery solution of the gastric contents, and the mixture evaporated. By proceeding in this manner we are certain that the hydrochloric acid, as well as all of the organic acids, has been neutralized in the residue. The alkalinity of the ash is the measure of the previously present organic acids. By means of this modification the Hehner-Maly method is also of value in estimating the higher fatty acids.

If it be desired to estimate the higher fatty acids by means of this procedure, the *unfiltered* gastric contents must be employed, since these acids (with the exception of butyric acid) on account of their insolubility, are simply suspended in the gastric contents, and would consequently remain upon the filter.

Determination of the Free Hydrochloric Acid or the Acid Excess ("*d*," p. 452).—Mintz's method of titration (that of adding a $\frac{N}{10}$ NaOH solution to the gastric juice from a buret until we fail to get the usual color reaction for free hydrochloric acid) is the best. (See p. 449 et seq.) Phloroglucin-vanillin is the most highly recommended of the reagents by Mintz. It requires but a few drops of the gastric contents, it is not influenced by any organic acid, and the final reaction is sharply defined. The necessity of heating each time the end-reaction is tested for makes the method tedious. Hence, it has not found much favor. A still more convenient method than that described upon p. 449 is to add 25 to 30 drops of phloroglucin-vanillin to the 10 cc. of gastric contents before titrating, for then, by heating the end of a glass rod moistened in the contents, we can observe the reaction directly. Of course, the glass rod should be cooled and washed carefully each time.

Another reaction, the addition of methyl-violet to normal gastric contents, and then $\frac{N}{10}$ NaOH solution until the blue color produced changes again to violet, has not given the author any satisfactory results, because it is so difficult to recognize the final reaction. But the end-reaction may be very well recognized with Congo-paper, adding the $\frac{N}{10}$ NaOH solution until the Congo-paper is no longer colored blue. Riegel recommends this method. The drop method is still more convenient, carrying the fluid in a platinum loop to the Congo-paper. Congo-red cannot be added to the gastric juice, because it is precipitated by acids. In order to shorten the method a portion of the gastric juice may be used for a rapid approximation, and to the rest merely the amount necessary may be added, as judged from the preliminary trial. We must, however, remember that the titration with the phloroglucin reaction will not necessarily give the same results as with Congo-red, on account of the degrees of delicacy of the indicators, and also on account of the sensitiveness of Congo-red to organic acids.

Mironescu[1] has shown that the values for free hydrochloric acid, especially in the Ewald-Boas test-meal, do not change if the gastric contents are allowed to stand. This is due to the fact that the hydrochloric acid is secreted so gradually that it combines with the proteins as fast as it is produced. With test-meals containing more solid com-

[1] Therap. Monatsh., November, 1905.

ponents which are not so easily attacked by the acid, this is not the case. It is better then to perform the titration as soon as possible after the contents have been removed from the stomach.

Hoffmann's Method for Determining Free Hydrochloric Acid or the Concentration of Hydrogen Ions from the Reaction Velocity of the Hydrolysis of Methyl Acetate.—This method depends on the fact that hydrogen ions, and therefore free hydrochloric acid, act catalytically in increasing the velocity of many reactions. The reaction which is used is the conversion of methyl acetate into acetic acid and methyl alcohol. The increase in hydrolysis is expressed by the equation of Wilhelmy:

$$C \,.\, D = \text{log. nat.} \frac{A}{A - x},$$

where D equals the time, C a constant proportional to the concentration of the HCl, A the maximum amount of acetic acid which may be formed from the methyl acetate used, and x, the amount of acetic acid which is formed in the time D. From the amount of acetic acid which is formed in a certain time, the concentration of hydrogen ions may be calculated. Hoffmann uses two flasks, the one containing a known amount of methyl acetate in a known volume of hydrochloric acid of definite strength, and the other the gastric juice with the amount of methyl acetate used in the first flask. From this, since

$$C \,.\, D = \text{log. nat.} \frac{A}{A - x}, \qquad C_1 \,.\, D = \frac{A}{A - x_1},$$

where x and x_1 are the concentrations of the acetic acid formed, C and C_1, the corresponding constants for the reaction velocity, and the other factors the same as in the first equation. If the time in both reactions be the same, D is eliminated from the equation. A is known. x and x_1 are known from the titration of the two solutions. One, therefore, obtains from the equations the values C and C_1. As the constants C and C_1 are propostional to the strength of the hydrochloric acid, one obtains from C, C_1 the concentration of the hydrochloric acid in the gastric juice. As the estimation is concerned merely with the calculation of the relations of C and C_1, one may use ordinary logarithms instead of natural ones. It is remarkable that this ingenious method which is free from the errors of others, and yet not complicated, thus far has not been used clinically.

Determination of the Hydrochloric Acid Deficit in a Gastric Contents which does Not Give a Reaction for Free Hydrochloric Acid.—By hydrochloric acid deficit we mean the amount of HCl which must be added to a definite volume of the stomach-contents in order to bring out the color reactions for free hydrochloric acid. This figure varies, of course, on the one hand, with the amount of proteins and peptones present, and perhaps with the alkaline components of the secretion, all of which combine with the acid; and, on the other hand, with the amount of hydrochloric acid already attached to the proteins. We might, therefore, call it a deficit in HCl saturation. To determine this deficit we add a $\frac{N}{10}$ HCl solution from a buret to 10 cc. of stomach-contents until the reaction for free hydrochloric acid is obtained in the mixture; this reaction is indicated most accurately by phloroglucin-vanillin or Congo-red.

Determination of the Chlorids of the Gastric Contents.—O. Reissner[1] has pointed out that the estimation of the combined chlorin or of the neutral chlorids has a certain diagnostic significance in the recognition of gastric carcinoma. He has found a greater increase in the chlorids in this disease than in other affections of the stomach, a fact which is the more striking since the secretion of hydrochloric acid is usually greatly diminished in gastric cancer. (See p. 464.) Reissner believes

[1] Zeit. f. klin. Med., vol. xliv.

this to be due to the neutralization of the hydrochloric acid, provided such be secreted at all, by the alkaline juice of the carcinoma, and to the chlorids contained in this cancerous secretion. If it be desired to estimate the chlorids in this connection, the directions will be found in the description of the method of Lütke-Martius (p. 455). In carrying out this procedure the modification of Reissner must be employed. (See p. 456.) By this method Reissner found that in other gastric diseases 100 cc. of gastric contents corresponded to a chlorid value of 24 to 40 cc. of $\frac{N}{10}$ silver solution; while in carcinoma the chlorids in the same quantity of gastric contents required 50 to 70 cc. of $\frac{N}{10}$ silver solution. It has not been determined whether gastric ulcer resembles carcinoma in this respect.

Quantitative Determination of the Total Organic Acids of the Gastric Contents.—The amount of total organic acids may be calculated after an Ewald test-breakfast by subtracting the hydrochloric acidity, as found by Lütke-Martius' method, from the total acidity, allowing, of course, that the acid salts do not play much of a part in the acidity. Martius considers that normally organic acids are absent during the digestion of the test-breakfast in the stomach (see p. 457 et seq.); hence, this remainder should equal nil.

The organic acids may also be estimated by Hehner-Maly's method (p. 457). This gives the acidity due to the organic acids directly.

Quantitative Estimation of Lactic Acid.—Strauss' modification of Uffelmann's method (p. 451) is practical and sufficiently accurate for the quantitative estimation of the lactic acid in the gastric contents. Boas[1] employs the iodoform reaction (p. 451 et seq.) when a more accurate estimation is required. The amount of iodin required to change the aldehyd formed from the lactic acid to iodoform is determined by titration.

If there be required a more accurate quantitative estimation of these acids than can be obtained by the Strauss modification of Uffelmann's test, the Hehner-Maly method for the organic acids may be employed (p. 457); for other organic acids have the same diagnostic significance as lactic acid, and are quantitatively, at least, subordinate.

Practical Utilization and Choice of the Quantitative Methods for the Determination of Acids.—At first sight the most accurate methods would seem absolutely essential for correct gastric diagnosis. We should then, naturally, select Lütke-Martius' or Sjöqvist's method to determine the total HCl secreted, Leo's method for the acid phosphates, Mintz's for the excess of acid, *i. e.*, the acid deficit according to Mintz, and, finally, Boas', for the determination of the lactic acid. But, as a matter of fact, none of these methods is absolutely accurate, and so many methods would make gastric examination too complicated and tedious for practical use.

Fortunately, in practice it is much more simple. The acidity due to acid phosphates is of no practical importance for titration if we employ Ewald's test-breakfast. (See p. 462.) The investigations of Moritz[2] and Martius show that the total acidity is almost entirely made up of the organic and hydrochloric acids.

The hydrochloric acids are composed of hydrochloric acid combined with the proteins, and of the free acid, reacting to Congo-red and phloroglucin-vanillin. A few examples will show that (if these facts be considered) even a simple acidity titration of the gastric contents furnishes considerable information about the gastric chemistry, provided the qualitative tests have been already performed.

Let us assume a case where the tests for free hydrochloric acid are negative. The total acidity is found to be quite high, *e. g.*, 0.25 per cent. in terms of HCl. We may then be pretty certain that most of this high acidity is due to free organic acids, and that the hydro-

[1] Deut. med. Woch., 1893, No. 34.
[2] Deut. Arch. f. klin. Med., 1889, vol. xliv, p. 279.

chloric-acid secretion is slight. If the lactic-acid test be very marked, if the odor of butyric or acetic be strong, and if the stomach-contents contain an abundance of bacteria, this assumption is practically proved. Conversely, if the hydrochloric-acid reaction be very pronounced, the lactic-acid reaction very faint or absent, and the acidity very high, in all probability there is an abnormal or excessive secretion of free HCl. If the acidity be relatively low and the hydrochloric-acid reaction positive, the probability is still greater that the acidity depends largely upon free hydrochloric acid. The titration for the total acidity is valuable, quite independent of the tests for free hydrochloric acid, for it indicates the maximum limit of HCl which is possible. For example: If the acidity be 0.08 per cent. (calculated as HCl), we are sure that the amount of free hydrochloric acid is not more than 0.08 per cent. anyway; which means that it is considerably diminished.

The excess or deficit of acid (see p. 458 et seq.) is easily estimated and gives us an important insight into the gastric chemistry. Some writers, as is well known, consider that in the determination of hydrochloric acid—the free hydrochloric acid—is the important part to be estimated, because in artificial digestion that is the only part which is effective. Others, on the contrary, consider that the free HCl can be neglected, as being, so to speak, useless, while the hydrochloric acid which is combined with the proteins is the important part, because it is accomplishing digestion in the stomach. Both are probably correct in a measure. The combined acid is doing the work, but the presence of a moderate excess is a favorable sign. It shows that there is enough to saturate the proteins and still leave more ready for anything else to be digested. The excess also aids in the antiseptic function of the stomach. But at the same time the hydrochloric acid deficit cannot be considered to measure an actual deficiency for the organism. On the other hand, the author wishes to warn against the overestimation of the value of finding free hydrochloric acid. Certain writers believe that the presence of the acid in the gastric contents is the principal factor in the pathology of the stomach. Both here and during the discussion of the value of the desmoid reaction the author wishes to point out that the finding of free hydrochloric acid after the usual test-meal, one which contains a minimal amount of food, and may, therefore, not be compared to those after an ordinary meal. This has been repeatedly observed after siphonage following a full meal. The amount of free hydrochloric acid to be found in the siphonage after a full meal with healthy individuals is often very different. Sometimes free hydrochloric acid is present, sometimes not, according to the phase of digestion at the time of siphonage. With a patient with only moderate digestive powers, the boundary between the presence or absence of free hydrochloric acid may shift from one examination to another. Moreover, it has been shown in recent investigations that peptic digestion may take place in the absence of free hydrochloric acid, providing the total acidity be sufficient. According to A. Müller,[1] the dog digests perfectly in the absence of free hydrochloric acid.

Schütz[2] also points out the relatively slight importance of free hydrochloric acid, and shows that with sufficient total acidity, peptic digestion may take place, even when the deficit in free hydrochloric acid is con-

[1] Arch. f. klin. Med., 1907, vol. lxxxviii, No. 4–6.
[2] Wien. klin. Woch., 1907, No. 44, and Wien. med. Woch., No. 41 and 42.

siderable. Rosenberg[1] has found that peptic digestion takes place without the presence of free hydrochloric acid.

The author believes, as the result of the consideration of the above-mentioned investigations, as well as the results which he has obtained with the desmoid test, that the constant fixing of the attention on the presence or absence of free hydrochloric acid has retarded very materially the progress of gastric pathology and diagnosis. Many cases of gastric carcinoma have, for example, been missed through the common and erroneous assumption that in this condition no free hydrochloric acid is to be found.

A comparison of the total acidity, as indicating the degree of acid secretion, with the excess of acid or acid deficit, will aid in determining the condition of the other gastric functions, especially the motility and the power of absorption. For example: If the total acidity be high, and we suppose that this is mainly due to hydrochloric acid secreted, and if further examination reveal no excess or only a slight excess of hydrochloric acid, or perhaps even an acid deficit, the high acidity can be due only to a deficient motility and absorption, so that much of the proteins remained in the stomach. A low total acidity with an excess of hydrochloric acid proves, on the contrary, that the motility and the absorbing power of the stomach are excellent.

If a qualitative examination of the gastric juice show that lactic acid is present, it may be quantitatively determined by Strauss' method (p. 451), the result deducted from the total acidity, and the remainder of the acidity calculated as above. Generally speaking, when much lactic acid is present, we find low HCl values and only combined HCl, *i. e.*, diminished secretion and diminished motility.

One may draw important conclusions without employing the difficult determination of free hydrochloric acid (Sjöqvist, Leo, Lütke-Martius, Hoffmann) by a simple determination of the total acidity. One may also determine the partition of hydrochloric acid and of lactic acid according to the method of Denigés. The method is described fully in his Précis de chimie analytique, Paris, A. Maloine, 1903.

PHYSIOLOGIC RELATIONSHIP OF THE ACIDS OF THE GASTRIC JUICE

Under physiologic conditions, one hour after Ewald's test-breakfast we find that the total acidity of the gastric juice varies between 0.15 and 0.2 per cent. (calculated in terms of HCl). The hydrochloric-acid tests with methyl-violet, tropæolin, and phloroglucin-vanillin all react positively; the lactic-acid test is negative. In healthy individuals Martius has shown that these values for the total acidity during the whole of the digestion correspond fairly accurately to the amount of hydrochloric acid secreted (estimated by Lütke-Martius' method). This proves that the organic acids are absent, and, at the same time, that the acid phosphates influence the total acidity but very little. The occurrence of organic acids in the stomach during the digestion of an Ewald test-breakfast is pathologic if we disregard the very slight amount of lactic acid which the test-breakfast itself contains. As a matter of fact, the antifermentation action of the hydrochloric acid inhibits the formation of these organic acids. Miller claims that lactic acid fermentation will cease if the amount of hydrochloric acid con-

[1] Zeit. f. klin. Med., 1905, lvi, p. 449. Note in Centralbl. f. allg. Path., 1905, No. 21.

tained in the mixture amount to 0.16 per cent., and Cohn puts it even as low as 0.07 per cent. Schüle[1] has contributed valuable facts in regard to the normal course of the acidity of the gastric juice and its individual components with different diets. He pictures the following curves (Fig. 208) to show the relations of the acidities after the ingestion of an Ewald test-breakfast.

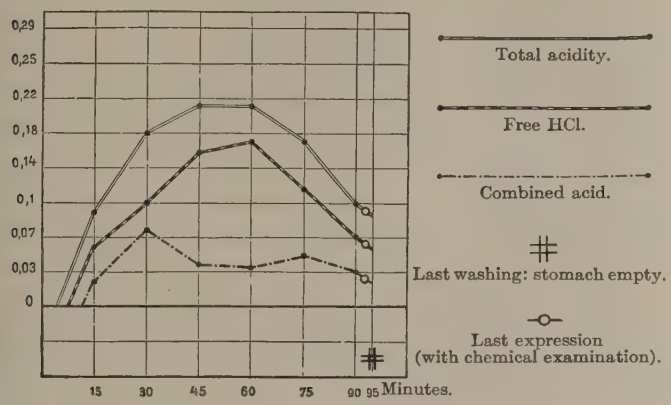


Fig. 208.—Course of the acidity of the gastric juice after a test-breakfast of 300 gm. of tea and 50 gm. of milk-bread (after A. Schüle).

We quote his observations upon healthy persons in the following:

"1. The values of the free as well as of the combined HCl and of the total acidity often differ considerably in the same individual and in different people, without any demonstrable cause. 2. The maximum of free HCl varies between 0.05 or 0.07 and 0.2 per cent.; the combined acids, between 0.012 and 0.11 per cent. The maximum of the total acidity lies, in round figures, between 30 (0.11 per cent. HCl) and 70 (0.26 per cent. HCl) at the height of digestion. 3. The height of digestion occurs sixty minutes after an Ewald test-breakfast, varying in individual cases from forty-five to seventy-five minutes. 4. The upper limits of these figures must be regarded as pathologic for many individuals with sensitive gastric mucous membranes."

Diagnostic Notes upon Acid Contents of the Gastric Juice

So long as we do not attempt to draw conclusions in regard to the volume of the secretion from the percentage of acidity (see p. 479), experience teaches us as follows:

(*a*) Normal hydrochloric acid secretion is present:
- (1) Very often in gastric ulcers, and in the pyloric stenosis due to a healed gastric ulcer.
- (2) In some of the gastric neuroses.
- (3) In simple atony of the stomach.

(*b*) The hydrochloric acid secretion is found to be increased:[2]
- (1) In the majority of the cases of gastric ulcer.
- (2) In motor insufficiency of the stomach (Schreiber) with maintained secretion of acid.

[1] Zeit. f. klin. Med., 1895, vol. xxviii.

[2] If the free hydrochloric acid after an Ewald test-breakfast exceed 0.2 per cent., or if the total acidity amount to more than about 70 (0.26 per cent. HCl), we may speak of it as an increased secretion. Pathologically, total acidity as high as 0.8 per cent. has been observed, due chiefly to HCl, but values over 0.35 per cent. are rare.

(3) In diseases of continual hypersecretion,[1] where the secretion continues to be excessive after the removal of the meal.[2]
(4) In simple hyperacidity and hypersecretion where the increased hydrochloric-acid production occurs (in contrast to (3)) only during digestion, and (in contrast to (2)) without motor insufficiency.[3]
(5) In temporary hypersecretion (gastroxynsis). This occurs in nervous individuals, as a result of severe mental exertion, associated with migraine, acid vomiting, and all sorts of nervous disturbances. In this group belongs the hypersecretion first described by the author as occurring in the gastric crises in locomotor ataxia.
(6) In the early stages of chronic gastric catarrh.
(7) In some types of mental disorders.

(*c*) Diminished secretion of hydrochloric acid occurs:
(1) In anemic conditions, especially in the severe forms.
(2) In most cases of chronic gastric catarrh.
(3) In some disorders of the stomach developing in the course of general neuroses (neurasthenia).
(4) In some types of mental disorders.
(5) In continued icterus.
(6) In some chronic cachexias, *e. g.*, tuberculosis of the lung (not constant).
(7) Sometimes in diseases with congestion (heart disease, emphysema).
(8) At times in chronic nephritis.
(9) After prolonged use of alkalis and saline purgatives.
(10) In chlorin hunger[4] after the prolonged exclusive use of milk.
(11) Not seldom in diabetes mellitus.

(*d*) Free hydrochloric acid is absent in those conditions which are mentioned under (*c*) when the disorder is very pronounced, and, besides this, more or less typically:[4]
(1) In severe febrile, especially infectious, diseases.
(2) In carcinoma of the stomach.
(3) In atrophic gastric catarrh.
(4) In pernicious anemia. Here probably with a distinct decrease in the total acidity there is a defective absorption of iron (the cause of the anemia) in consequence of a chronic gastric catarrh. (See section on Pernicious Anemia in Examination of the Blood.)

In reality, numerous deviations are observed in all the conditions which are grouped in the above scheme.

We are justified in attaching great weight to the absence of free hydrochloric acid, *i. e.*, to a negative result in the color tests, for the diagnosis of gastric carcinoma, especially if this HCl absence can be noted regularly before any tumor can be felt. Nevertheless, the presence of free HCl does not necessarily exclude the diagnosis of a carcinoma. One case was especially instructive to the author in this respect. For months he found a normal amount of hydrochloric acid after a test-breakfast, although the patient presented a carcinomatous stenosis of the pylorus with marked nocturnal retention of food. In the retained material he found a very greatly increased amount of hydrochloric acid (up to 0.4 per cent.). Other writers have reported similar observations. Moreover, other disturbances cited in groups *c* and *d* are frequently accompanied by a complete absence of the

[1] See p. 446 for the amount of secretion occurring in the fasting stomach of healthy individuals.

[2] The most important differential diagnostic sign between true continued hypersecretion (gastrosuccorrhea) and cases where prolonged secretion of the gastric juice occurs, due to motor insufficiency, with or without stenosis of the pylorus, is the condition of the fasting stomach in the morning, after it has been completely emptied the evening before. If it, then, the next morning contain fluid rich in hydrochloric acid, the condition is one of true hypersecretion.

[3] There is really no sharp boundary line between these two conditions. If merely the percentage of acid contained be too high, we call it hyperacidity; but if, besides this, the volume of the gastric juice be also increased, we call it also hypersecretion. Hyperacidity and hypersecretion may occur independently, or they may result from a motor insufficiency (stagnation).

[4] The more exact quantitative methods for testing the total and the combined hydrochloric acid, *e. g.*, Lütke-Martius, would still generally show that a slight amount of hydrochloric acid was secreted. Yet the secretion may even be completely suppressed and the gastric juice then give a neutral or weakly alkaline reaction.

color reaction for free HCl, so that an absence of free HCl can hardly be claimed as distinctive of gastric carcinoma.

(*e*) A considerable amount of organic acids, especially of lactic acid, occurs only when hydrochloric acid is absent and when, at the same time, motor insufficiency exists, especially when the latter depends upon some stenosis of the pylorus. This is the reason that a considerable amount of lactic acid in the gastric contents strongly suggests a carcinoma.

Testing of the Digestive Power of the Gastric Juice; Examination for Pepsin

The digestive power of the filtered stomach-contents from the expressed test-breakfast depends, on the one hand, upon the amount of pepsin contained, and, on the other hand, upon the amount of free acid contained, especially free hydrochloric acid. Negatively, the digestive power of the gastric juice is influenced by the presence of substances inhibiting digestion. Artificial digestion is the only means at our command to estimate the amount of pepsin. This furnishes also indirect evidence of the amount of acid contained in the gastric juice.

For artificial digestion we usually employ fibrin stained with carmin (Grützner), or disks of coagulated egg-albumen.

The fibrin is best prepared by beating freshly drawn ox-blood. The stringy coagula are washed in running water until decolorized, and then cut into small pieces of uniform size, which are then placed in alcohol for several days. They are then transferred for one to two days into a $\frac{1}{4}$ to $\frac{1}{2}$ per cent. ammoniacal solution of carmin, which should contain as little excess of ammonia as possible and kept cool until they are thoroughly stained, washed in water until the wash-water is no longer colored, well squeezed, and then preserved in glycerin. Before being used they should be carefully washed in water to free them of glycerin.

The egg-albumen disks are prepared by boiling an egg hard,[1] and then with a cork-borer punching out the white cylinders of about 5 mm. diameter. These cylinders are sectioned with a razor into small disks of 1 mm. thickness, preserved in glycerin, and also washed off before using.

For the digestive test a few bits of fibrin or some egg-albumen disks are put into a test-tube with a measured quantity of the gastric contents and the tube then set in an incubator. The digestion of the fibrin releases the carmin and becomes evident from the red color of the fluid. The digestion of the egg-albumen always progresses much more slowly. It shows itself first in the rounding of the edges of the disk, followed gradually by complete solution.

The following methods are to be recommended for a more accurate quantitative examination:

Hammerschlag's[2] Method for Estimating Pepsin.—Ten cc. of an approximately 1 per cent. filtered solution of egg-albumen[3] in 0.4 per cent. HCl are poured into two tubes. To one 5 cc. of gastric contents are added, and to the other 5 cc. of distilled water. They are both set in the incubator. An hour later the albumin in both tubes is estimated volumetrically according to Esbach's method (p. 615 et seq.). The difference between the precipitate of albumin in the two tubes is equal to the amount of albumin which has been digested, and forms, therefore, a measure of the peptic activity of the gastric juice. The square root of the amount

[1] The egg should be boiled only long enough to coagulate the egg-albumen completely, otherwise it becomes too difficult to digest. The necessary boiling period must be found experimentally.

[2] Internat. klin. Rundschau, 1895, vol. viii, No. 39.

[3] Fresh egg-albumen contains about 13 per cent. of dry protein and should therefore be diluted about 13 times in order to make approximately a 1 per cent. solution of egg-albumen.

of pepsin is proportional to the quantity of albumin dissolved, according to Schütz,[1] Borrissow,[2] and Linossier.[3] The objections to this method are that the Esbach test is not very accurate, and that the albumoses are also partly precipitated. The error in regard to the precipitation of the albumoses is negligible, since they come down so finely divided and settle with so much difficulty that practically they do not influence the amount of the sediment to any appreciable extent. The method is sufficiently accurate for practical utility in judging of the quantity of pepsin in the stomach-contents. It would be better, however, to employ a diluted gastric juice, for the reasons given in the description of Mett's method.

Mett's[4] Method of Pepsin Determination.—Glass capillary tubes, from 1 to 2 mm. in diameter and 20 to 30 cm. in length, are filled by suction with the fluid portion of fresh egg-albumen. In order to avoid accidental variations in the egg-albumen, the whites of several eggs should be mixed, filtered through gauze, and the fluid portion of the mixture employed. These filled capillary tubes are closed with bread-crumbs and placed horizontally in a boiling water-bath, in order to coagulate the albumin quickly. At the end of five minutes they are withdrawn, wiped off, and their ends plunged into melted paraffin, in order to prevent drying. A number of these capillary tubes may be prepared and kept in stock; but before they are employed, it should be noted that the cylinders of albumin are still in contact with the walls of the tube and have not dried out and contracted, in which case they are unfit for use. At first the capillary tubes contain countless bubbles, which, however, gradually disappear, and in two days they are ready for use. They are then cut into lengths of about 2 cm. with a file, and two of them are placed in a little dish with 5 cc. of the acidulated gastric contents, the pepsin value of which is to be determined. The manner in which the digesting mixture is to be prepared from the gastric contents will be subsequently stated. Digestion is now allowed to proceed in the incubator; it is manifested by the fact that the albumin gradually disappears from the ends of the tubes, the disappearance gradually becoming more rapid.

According to Nirenstein and Schiff,[5] the length of the cylinder of albumin digested by any gastric juice is proportional to the duration of digestion and independent of the diameter of the capillary tube, provided that the length of the digested cylinder does not exceed 7 mm. within the time of observation.[6] If the digested cylinder exceed 7 mm., however, the length is not proportional to the time, since the digestion beyond this point seems to proceed more slowly as a result of the difficulty of the diffusion of the digested products into the surrounding fluid. To obtain a correct quantitative estimate of the amount of pepsin in the gastric contents we must consequently keep within this limit, which may be done by preparing the digesting mixture in the manner to be given presently, and measuring the mass of albumin dissolved at the end of twenty-four hours. This may be roughly estimated macroscopically, and more exactly by a low-power microscope provided with an objective micrometer. If two capillary tubes be employed, their four ends furnish four digestion-lengths, from which an average may be obtained.

For solutions of pure pepsin, Schütz has discovered the law that the relative quantities of pepsin in digesting mixtures containing the same quantity of hydrochloric acid are proportional to the squares of the quantities of albumin digested in the same time. Borissow has confirmed this, particularly in reference to the method of Mett, so that in this connection Schütz's law is that the square of the length of the digested cylinder of albumin is proportional to the pepsin concentration of the solution. From the studies of Nirenstein and Schiff, however, this is true only for the less concentrated pepsin solutions. If the quantity of pepsin in the digesting fluid be so large that more than 3.9 mm. of albumin are digested in twenty-four hours, the law of Schütz does not obtain reliable values for the quantity of pepsin in any gastric juice by Mett's method; then it must be diluted so that the digestion length will not exceed 3.9 mm. in twenty-four hours. We have already given two reasons which make it necessary to dilute the gastric juice in determining the amount of the contained pepsin. A third and far more impor-

[1] Zeit. f. physiol. Chemie, 1885.
[2] Quoted by Samoiloff, Arch. des sci. biol., St. Petersburg, vol. ii, No. 5.
[3] Jour. de phys. et de path. gen., 1899, vol. i, No. 2.
[4] I. A. D., Petersburg, 1889, from Pawlow's laboratory.
[5] Arch. f. Verdauungskrankh., 1903, vol. viii, part 6.
[6] Schütz and Huppert have found that the amount of the products of digestion are proportional to the square root of the time of digestion. (See Volhard's method, p. 468.)

tant reason for such dilution, to which the author referred in a previous edition of this book, and which has recently been more critically discussed by Nirenstein and Schiff, is that the gastric juice, as obtained from the patient by filtering the gastric contents after a test-breakfast, always contains an uncertain quantity of substances which inhibit pepsin digestion. These inhibiting substances are the products of the peptic digestion itself; Nirenstein and Schiff state that they are particularly the dissolved carbohydrates and also sodium chlorid. Gastric juices with diminished amounts of hydrochloric acid, on account of the large quantities of carbohydrates which they contain, are the richest in such inhibiting substances. The important rôle played by these inhibiting substances is shown by the fact that, if Mett's method be carried out with different slight dilutions of the same gastric juice, the relative pepsin values, as obtained by applying Schütz's law to the digestion lengths, never agree with the relative amounts of pepsin as calculated from the dilution. As a matter of fact, it will be found that if the gastric juice be diluted to two or three times its volume, a higher digestive value will frequently be obtained than if the undiluted juice be employed. This is evidently due to the fact that in such a dilution the diminished amount of pepsin is more than compensated for by the weakening of the activity of these inhibiting substances. The presence of these substances consequently gives rise to conditions beyond computation, which make it impossible to arrive at accurate conclusions if the pepsin value be calculated from the pure gastric juice.

It is apparent that the way to avoid this difficulty is to eliminate this inhibitory action by diluting the gastric juice. In a previous edition of this book, having this end in view, the author recommended a tenfold dilution of the total gastric juice in diluted hydrochloric acid. Nirenstein and Schiff, however, have shown that it is better to carry the dilution still further. They recommend a sixteenfold dilution with $\frac{N}{20}$ hydrochloric acid (= 0.18 per cent. HCl), and state that Schütz's law obtains with this and all further dilutions. The latter requisite is absolutely necessary if we wish to have a relative expression for the quantity of pepsin as estimated from the digestion length. This marked dilution also decreases the amount of pepsin in the mixture, so that the digestion length is kept within the limits of Schütz's law (3.9 mm. in twenty-four hours). The author must, nevertheless, observe that this is not always the case with a very active gastric juice, so that if the digestion length exceeds 3.9 mm. with a sixteenfold dilution, it becomes necessary to repeat the pepsin test with a dilution of 1 : 32.

According to Nirenstein and Schiff, the method of Mett will consequently be carried out in the following manner if exact quantitative results are to be obtained: 1 cc. of the filtered gastric contents is diluted with 16 cc. of $\frac{N}{20}$ HCl (=0.18 per cent. HCl). Two Mett's tubes are then laid in this mixture which is placed in the incubator. At the end of twenty-four hours the digestion lengths are read and the mean digestion length calculated. The square of this digestion length is the measure for the relative amount of pepsin in the sixteenfold diluted gastric juice, and this number, multiplied by 16, gives the relative amount of pepsin in the undiluted gastric juice. In those cases in which the length of the digested cylinder of albumin exceeds 3.9 mm. in length, in spite of the sixteenfold dilution, the estimation must be repeated with a dilution of 1 : 32. By squaring the digestion length as before, and multiplying this quantity by 32, the relative amount of pepsin in the undiluted gastric juice will be obtained. In order to facilitate matters it is better to perform several tests at the same time with dilutions of 1 : 16, 1 : 32 and 1 : 64. One has then the opportunity of observing whether the results conform with the law of ferment action. It is clear that in this method of estimation the unit of the relative amount of pepsin will be that quantity of pepsin by which 1 mm. of albumin in a Mett's tube will be digested in twenty-four hours with an acidity of 0.18 per cent. free hydrochloric acid. In this estimation we do not consider the absolute quantity of the pepsin, but simply the degree of its concentration, for the result of Mett's method is the same whether large or small quantities of the digesting mixture be employed; at least for quantities above the 16 cc. above recommended. By employing this method Nirenstein and Schiff have found striking differences between individual gastric secretions, which vary between 0 and 256 pepsin units. A content of 0 to 70 is to be considered low; 70 to 150, average, and 150 to 256, high. The pepsin concentration is consequently entirely independent of the amount of acid in the gastric juice, as we might expect from the fact that physiologists have demonstrated a different localization for the formation of pepsin and hydrochloric acid in the gastric glands.

Against the Mett estimation has been objected that the measurements of the

digested albumin are so small that the error through squaring and multiplication is so magnified that it plays much too great a part for an accurate method. A much more serious objection is that of Arrhenius (Immunochemie, Leipzig, 1907). This investigator has shown that when alkaline solutions containing phenolphthalein are allowed to diffuse into a capillary tube filled with gelatin, the law of square roots holds for diffusion, so that with a solution of alkali of a concentration of 4, the diffusion takes place twice as rapidly as for a concentration of 1. From this it follows that the results of Nirenstein and Schiff are only apparent, as the digestion is dependent on the rate of diffusion. One must, however, allow that if the diffusion were the predominant factor, the law would still hold for high concentrations of pepsin, which is not the case. There must be, therefore, in the higher concentrations, an inhibition. With Mett's method, taking into account the diffusion, one is unable to show that the Schütz law holds, nor can one estimate the number of pepsin units, as the results, taking into consideration the amount of diffusion, are in agreement with a simple proportion between the amount of peptic action and the concentration of the solution.

Volhard's Method for Estimating Pepsin.—This method makes use of the fact that casein, dissolved in hydrochloric acid of the strength found in the gastric juice, is completely precipitated by sodium sulphate. If, therefore, one allows pepsin to act on a solution of casein at 40°, the more the casein is digested by the pepsin, the less will be the precipitate produced by sodium sulphate. Thomas and Weber have estimated the amount of casein left undigested to determine the degree of pepsin action. The technical difficulty of the estimation of the weight of the precipitate is avoided by Volhard, by making a titration of the acidity of the filtrate. He found that an amount of hydrochloric acid is combined with the casein which is precipitated, while a proportional amount remains in the filtrate. If one, therefore, estimates the acidity after precipitating the unchanged casein solution and compares with this the acidity of a partially digested but otherwise identical casein solution, the increase in acidity of the latter is a measure of the peptic digestion. Volhard finds proof for this in that the amount of casein precipitated is proportional to the deficit in the degree of acidity, and corresponding to Schütz's rule, for equal intervals of time, the increase in the acidity of the filtrate, within certain limits, is proportional to the square root of the amount of ferment contained in the solution. If, therefore, one wishes to estimate the amount of pepsin contained in the solution, one allows a definite volume of the gastric juice to stand with a definite volume of a known HCl casein solution at 40° C., precipitates the solution with sodium sulphate after a definite time, and titrates the filtrate after precipitating the unchanged casein with sodium sulphate. The same operation is repeated with undigested casein solution. The difference in the acidity of the two solutions, when squared, gives the relative amount of pepsin contained in the digestion mixture.

As, however, the ferment law is valid only within certain limits, one cannot determine the amount of pepsin from a single test, but must perform several with different concentrations of gastric juice, and only those tests can be used which correspond to the ferment law. For example, if 3 tests be digested for an hour, only those tests can be used when the first contains 1 cc. of gastric juice, the second 4 cc., and the third 9 cc., and the digestive products, or what is the same thing, the increase in acidity are in the ratios of 1 : 2 : 3. If the times of digestion have been unequal, one must, according to Volhard, who follows the results of Schütz and Huppert, take into consideration that the digestive products are not alone proportional to the square root of the ferment concentration, but to the time of digestion, and that the increases in acidity behave according to $\sqrt{ft}$ (f = relative amount of ferment or amount of gastric juice; t = time of digestion), or, in other words, the relation between increase in acidity and ft must be a constant. (See p. 469.)

Technic.—Casein solution. 100 gm. of finely granular casein (Rhenania) are mixed with 100 cc. of distilled water and well shaken. Eighty cc. of normal sodium hydroxid are added, and diluted to 2000 cc. The mixture is gently warmed until the casein is completely dissolved, and then heated quickly to 85° to 90° in order to destroy any proteolytic ferment which may be present. The solution is allowed to cool, and a few cubic centimeters of toluol added. The solution may be kept indefinitely.

Volhard uses long-necked digestion flasks with two marks on the neck at 300 and 400 cc.

The test is made in the following way (Löhlein): 11 cc. of normal hydrochloric acid are measured into three digestion flasks and diluted to 150 cc. with water. To the contents of each flask are added 100 cc. of the standard casein solution. The mixture is shaken. No precipitation may take place. To each flask is added

a definite but varying amount of the gastric juice (see later), best after the casein mixture is warmed on the water-bath to 40°. The whole is then diluted to 300 cc. The mixture is then digested for an hour in a water-bath at 40°. In order to stop the digestion it is necessary to add only 100 cc. of 20 per cent. sodium sulphate (up to the 400 cc. mark). This precipitates the undigested casein, and the hydrochloric acid which is in the soluble digested portion remains in the solution.

The acidity of 100 or 200 cc. of the filtrate is estimated with decinormal sodium hydroxid. The total acidity of the filtrate from an undigested test is determined once for all. This is subtracted from the acidity of the digestion tests, in order to determine the increase in acidity due to digestion. This acidity is, therefore, a measure of the digestive activity. The initial acidity of the gastric juice must naturally be subtracted from that of the digestion mixture. In spite of what has been said on p. 454, Volhard uses phenolphthalein as an indicator. In case of normal or hyperacidity Volhard employs 0.2, 0.8, 1.8 cc., or when sufficient gastric juice is to be had, 0.4, 1.6, and 3.6 cc. With juices containing no acid or of feeble acidity, 1.0, 4.0, 9.0, or 2.0, 8.0, and 18.0 cc. With these proportions it is altogether probable that at least two of the tests of each group will fall within the limits of the law of ferments. M. Schapiro[1] has made determinations in the author's laboratory with gastric contents of high ferment activity and much acid. The results are best with 0.1 and 5 cc. of gastric juice (0.1, 0.4,and 0.9 etc. with weak gastric contents, of low acidity, with additions of 5 cc. and more (4.9, 6.4, 8.1, relations of 0.1×7^2, 0.1×8^2, and 0.1×9^2) or 5.0, 7.2, and 9.8 (0.2×5^2, 0.2×6^2, 0.2×7^2).

In order to find out definitely what are the quantities of gastric juice which are necessary, Volhard says that one should use 10 times the smallest amount which is used in the determination of the coagulating ferment. For example, if the coagulation tests in dilution II (1 : 100), 0.9, 0.8, 0.7, up to 0.4 cc. are positive (coagulation) and dilution II (1 : 100), 0.3, 0.2, 0.1 cc. negative (no coagulation), the smallest coagulating amount is 0.4 cc. of dilution II = 0.004 cc. In this case, therefore, one uses for the tests 0.04, 0.16, and 0.36 cc. of gastric juice (relations of 1, 4, 9) in the form of undiluted unneutralized gastric juice. The gastric juice is measured out from a pipet which allows the measurement of 0.01 cc. The values for pepsin will then fall pretty closely within the laws for ferment action. With achylic or hypochylic gastric juices there is often not enough juice with which to perform the three tests. In this case we must be content with one test.

If a value within the ferment law has been found, the following calculation, according to Volhard, can be made.

If one assume as the ferment unit that amount of ferment which gives in one hour's digestion an increase of 1.0 cc. of decinormal alkali for titration, and designates by a the increase in acidity, then, according to the Schütz-Huppert rule, by using n cc. of gastric juice which contains x ferment units per cubic centimeter—

$$a = \sqrt{nxt}$$

$$\sqrt{x} = \frac{a}{\sqrt{nt}}$$

$$x = \frac{a^2}{nt} = \text{number of pepsin units in 1 cc. of the gastric juice.}$$

It is only questionable if it be right to assume that, in the above formula, the value a should be influenced by the square root, or, in other words, whether the reaction velocity for peptic digestion is a function of a square root. This so-called time law for pepsin (x) has not been perfectly proved. (See the Carmin Method.)

Volhard's has the advantage over Mett's method that with weak gastric juices values will be obtained when no digestion can be observed with Mett's tubes.

Grutzner's Carmin-fibrin Method for the Quantitative Estimation of Pepsin.[2]—This method, which was proposed in 1874 by Grützner for the determination of pepsin, and which was for a time quite superseded by other methods, is again receiving attention from clinicians since Grützner and Korn[3] have again pointed out the great simplicity of the method, and have shown that by it the pepsin ferment laws may be worked out more easily than with any other method. The principle of the carmin fibrin is that one allows a digestive juice to act on a fibrin stained with carmin for a certain length of time, and estimates colorimetrically the amount of pigment set free, by comparing it with carmin solutions of a definite concentration.

[1] M. Schapiro, Volhard's Method for Estimating Pepsin. Inaug. Diss., Bern, 1908.

[2] Pflüger's Arch., 1874, vol. viii, p. 542, and Habilitationsschrift, Breslau, 1875.

[3] Korn, Quantitative Pepsin Estimation, Inaug. Diss., Tübingen, 1902.

The intensity of the color is proportional to the ferment action. The method has the further advantages that it is not necessary to perform any particular manipulations, titrations, or weighings, and that on account of the easy digestibility of fibrin it takes but five to ten minutes.

The fibrin carmin is prepared as shown on p. 465. Preparation of the scale of colors. Ten different solutions of carmin are prepared:

The first	contains	0.1	cc.	1 per cent.	carmin	glycerin	and	19.9 cc.	water
The second	"	0.2	"	1	"	"	"	19.8 "	"
The third	"	0.3	"	1	"	"	"	19.7 "	"
The fourth	"	0.4	"	1	"	"	"	19.6 "	"
The fifth	"	0.5	"	1	"	"	"	19.5 "	"
The sixth	"	0.6	"	1	"	"	"	19.4 "	"
The seventh	"	0.7	"	1	"	"	"	19.3 "	"
The eighth	"	0.8	"	1	"	"	"	19.2 "	"
The ninth	"	0.9	"	1	"	"	"	19.1 "	"
The tenth	"	1.0	"	1	"	"	"	19.0 "	"

The Digestion Test.—As the intensity of the shades of color are proportional to the amount of fibrin digested, the degree of color gives directly the intensity of the digestion. The number of the comparison solution which is like the digestion mixture gives the amount of digestion in units where the unit of digestion is solution 1. Therefore, by this method the determination of the number of units is more simple than by any other. Five tests are made in test-tubes. Each test-tube contains, as nearly as possible, the same amount of swollen fibrin, which should not in any case exceed 0.5 gm. The amount of fibrin is estimated with the eye, or if one wishes to be more exact, is weighed after being pressed with the fingers. To these quantities of fibrin are added:

In test-tube	1	9.95 cc.	0.3 per cent.	HCl	+	0.05 cc.	gastric	juice
" "	2	9.90 cc.	0.3 "	HCl	+	0.10 cc.	"	"
" "	3	9.80 cc.	0.3 "	HCl	+	0.20 cc.	"	"
" "	4	9.55 cc.	0.3 "	HCl	+	0.45 cc.	"	"
" "	5	10.00 cc.	0.3 "	HCl	+	0.00 cc.	"	"

The test-tubes are allowed to remain at room temperature for twenty minutes and are shaken during this time every five minutes; the red color is then compared with the scale of colors. As the relative amount of peptic digestion is obtained directly from the color scale, one has an opportunity with this method to test the ferment laws with regard to the factors of reaction velocity and influence of concentration of ferment. From Korn's investigations it appears that the ferment activity may be estimated in a five-minute test. In case no interfering factors come in, the amount of pepsin in mixtures 1, 3, and 4 must be in the ratio of 1, 2, and 3, as the relative amounts of ferment are as 1, 4, and 9. If the tests do not agree, then smaller amounts of ferment, as a rule, must be employed. From the dilutions falling within the limits of the law of ferments, the content of enzyme is calculated in the following way. Supposing that the mixture 1 : 4 have fallen within the limit, so that after five minutes mixture 1 has a color intensity corresponding to I, 3, corresponding to II, and 4, to III. One takes any one of the mixtures, say, 3. This contains 0.2 cc. of gastric juice in 10 cc. = a dilution of 1 : 50. This mixture shows a digestive capacity of II. If we assume as the unit of peptic force the amount of color set free in five minutes as 1 (the expression peptic unit may give rise to error because the square root of the pepsin concentration, and not the concentration itself is proportional to the digestive capacity), such an undiluted gastric juice would contain $2 \times \sqrt{50}$ peptic units. If the ferment law is arrived at after only ten minutes, the number is to be divided by 2, as it has been found that ordinarily in weak concentrations the amount of digestion is proportional to the time, and not to the square root of this factor. Another method of using carmin fibrin is detailed on p. 472.

The Grützner method is one of the best which we have for the estimation of pepsin. The only disadvantage is that the solutions of carmin are not stable. This may be avoided by preparing them fresh from time to time. The author has endeavored to overcome this difficulty by preparing a solution containing picric acid and sodium rosanilin trisulphonate (Merck, non-toxic). A standard solution is prepared by mixing with 50 cc. glycerin, 2.5 cc. of a 0.1 per cent. glycerin solution of sodium rosanilin trisulphonate and 2.5 cc. of 0.05 per cent. alcoholic solution of picric acid. After finding that a solution of this diluted 1 : 10 gives the same color as the carmin solution x, and one has corrected the shade of color to the car-

min by the addition of the red or yellow components, standard solutions are prepared by using the original solution as solution 10 and adding to 10 test-tubes 1, 2, 3, 4, 5, 6, 7, 8, 9, cc. of the standard solution and diluting to 10 cc. with glycerin. These solutions are stable. Another method which the author has found useful is to stain the fibrin with Berlin blue instead of with carmin. The Berlin-blue solutions, as far as the author has been able to ascertain, are stable. As the so-called Berlin blue is not, strictly speaking, soluble in water, the fibrin must be so stained that the color is formed in the fibrin itself. In order to do this the fibrin is first immersed in a solution of potassium ferrocyanid, and subsequently in a solution of ferric chlorid. The solutions must be very dilute, for stronger solutions impair the digestibility of the fibrin. It has also been found useful to perform the test in the following way: Fibrin which has been preserved in glycerin, and which has been exposed neither to heat nor to the action of alcohol, is freed from glycerin by soaking in water and just covered with a 1 per cent. solution of potassium ferrocyanid, and allowed to stand for eight hours. The supernatant fluid is then poured off and measured. An equal volume of ferric chlorid solution of the following composition is then poured on, and the fibrin and solution transferred to a porcelain mortar, and well rubbed up until the protein is homogeneously blue in color. The dilute ferric chlorid is prepared by adding to 10 cc. of water 1 cc. of liquor ferri sesquichlorati diluted six times. The stained fibrin is well washed with water to remove excess of color and small particles of fibrin. The protein is then placed in glycerin and preserved. Fibrin obtained in this way does not lose its color or its capacity for digestion. The standard solutions for the comparison of the color are so prepared that the darkest solution (x) is made. This is done by dissolving Berlinblau (Grübler) to the desired tint in decinormal oxalic acid solution, and making other solutions containing 9, 8, 7, 6, 5, 4, 3, 2, 1, cc. of this solution to 10 cc. with decinormal oxalic acid solution. The solutions are stable so far as the author has been able to observe, for at least some months, provided they are kept in sealed glass tubes and protected from light.

Jacoby's Method for Estimating Pepsin.[1]—This method depends on the fact that a solution of ricin in 1 per cent. sodium chlorid, in consequence of the protein contained in it, is not clear, but with the addition of hydrochloric acid and pepsin the opalescence appears. The amount of gastric juice is determined which is sufficient to clarify such a ricin solution of a definite concentration. The details of the method will be found in a paper by Solms.[2] Ricin is now a comparatively inexpensive article of commerce. The "Vereinigte Chemische Werken," Charlottenburg, Salzufer 16, sell it with directions for performing the test. Apparently Schütz's law does not hold in the ricin test. This is due to the fact that we are here dealing with the minimum digestive capacity in which inhibitory factors probably do not play an important part.

Fuld's Method for Estimating Pepsin.[3]—This method is based on a principle similar to that of Jacoby. Fuld prepares a solution of edestin in hydrochloric acid, and determines the amount of gastric juice necessary for the complete digestion of the edestin. When the protein is completely digested, no ring of protein is formed by placing ammonia solution on top of the digestion mixture. In this method Schütz's law is not followed. It is a limit method, and the proportion between digestive action and amount of pepsin is a direct one.

Gross' Method for Estimating Pepsin.[4]—This method is similar to those of Jacoby and Fuld. A very dilute solution of casein in hydrochloric acid is used. The concentration employed is 0.1 per cent. This is prepared by heating 1 gm. of casein with 16 cc. of a 5 per cent. solution of hydrochloric acid (sp. gr., 1.114) made up to a 1000 cc. with water until the casein is dissolved. A number of test-tubes are filled with this solution, previously warmed to body temperature, and increasing amounts of gastric juice added. These remain at this temperature for a certain time, and the casein is precipitated by a solution of sodium acetate. The limit is determined when no precipitate is produced by adding this solution.

Schorer's Refractometric Method.[5]—G. Schorer has worked out a method in the author's clinic, using the Pulfrich immersion refractometer. The details will be found in the original paper. The method is based on the experiments of Obermeyer and Pick[6] who showed that during digestion of egg-albumen, the refractive index is not altered. The egg-albumen solution is prepared of a concentration of

[1] Biochemische Zeit., vol. i, No. 1 and 2.
[2] Zeit. f. klin. Med., 1907, vol. lxiv, No. 1 and 2.
[3] Münch. med. Woch., 1907, No. 29.
[4] Berlin. klin. Woch., 1908, No. 13.
[5] Inaug. Diss., Bern, 1908.
[6] Hofmeister's Beiträge, 1906, p. 331.

0.62 per cent., and of this, 40 cc. are mixed with 4 cc. of normal hydrochloric acid and 0.1 cc. of the gastric juice. The mixture is then made up to 50 cc. Ten cc. of this mixture are used for a refractometric determination, and the remaining 40 cc. are digested at 40° in a thermostat for twenty-four hours. Twenty cc. of the mixture are then mixed with 1 or 2 drops of azolithmin (Merck) solution, and then accurately neutralized with sodium hydroxid. Then a drop of 5 per cent. acetic acid is added. The color of the solution must now be distinctly red, not violet. A precipitate of acid albumin is produced. The mixture is now heated over a free flame to boiling. If the mixture lose its red color during boiling, a very small drop of acetic acid must be added to restore it. On cooling the solution, it is made up to 20 cc. and examined with the refractometer. The difference between the refractive index before and after digestion gives a measure of the amount of the latter. The results can be expressed either in units of pepsin or in units of digestive capacity. Such results can be obtained only when more than one test is made, and the results fall within the limits of the law of ferments.

CRITICISM OF THE CLINICAL METHODS FOR THE ESTIMATION OF PEPSIN, WITH SUGGESTIONS FOR CLINICAL METHODS

The newer methods for the estimation of pepsin fulfil to a certain extent the conditions for obtaining absolute values for the content of a gastric juice in pepsin. This is, however, possible only when the so-called ferment law is a quantitative one, and, secondly, when the experiments are so designed that the results are not disturbed by complicating factors. With regard to the course of the reaction by which pepsin digests proteins, the views of different investigators are at variance. Some assume that the reaction follows Schütz's law of squares, while other believe there is a strict proportion between the amount of ferment and the amount of digestion. It seems that the curve representing the action of pepsin is a complicated one, in which the action is rapid at first, and then rises less quickly. It would seem that in the beginning the reaction follows the law of simple proportion, and later there is a quadratic relation between the amount of digestion and the concentration of the pepsin. In the intermediate zone there is apparently no mathematical formula which will express the course of the reaction. If, however, the assumption be correct that with the minimal action of pepsin the simple rule holds of simple strict proportion, as in Jacoby's and Gross' methods, it would seem advisable to use these methods for clinical purposes. On the other hand, it appears to the author that it might be better to dispense altogether with the quantitative estimation of pepsin for clinical purposes, and to confine one's attention to an examination of the gastric juice as a whole with regard to its digestive capacity. The most important point for practical purposes is not to know what amount of pepsin is contained in a gastric juice, but to ascertain in and how, during a meal, this digestive juice exercises its function. A gastric juice theoretically rich in pepsin will not be of any value to the patient, if, for any reason, inhibitory influences, either from products of digestion or from antiferments, are at work. And, conversely, it is not necessary for a gastric juice to have any very great ferment activity to perform its functions quite perfectly if the inhibitory factors are absent. Hence to determine the actual conditions in the stomach, we must examine the gastric juice undiluted, and not rely on the determinations of pepsin. For this purpose, the best method is a modification of the carmin method which was described by the author in the earlier editions of this book. In this method exactness was not aimed at, but undiluted gastric contents were used. In cases of low acidity, it is wise to make a second test, making the total acidity

of the test up to 0.2 per cent. hydrochloric acid. The amount of gastric juice and the fibrin must be the same in both tests. In order not to increase the amount of the gastric juice unduly by the addition of acid, the latter must be added in a concentrated form, only the few drops necessary to bring the concentration of the acid up to the desired amount. This must be determined beforehand by a preliminary titration. Two further tests can be made, in which equal amounts of boiled and unboiled juice are used, and also equal volumes of gastric juice and water. In these cases also, the total volume of the mixture, the acidity, and the amount of fibrin must be alike. The object of these tests is to obtain information through the addition of water, and the destruction of the ferment regarding the presence of inhibitory factors. This information is of importance because such inhibitions may be the cause of gastric disturbances, due to the retention in the stomach of the products of digestion; and this may be relieved by increasing the motility of the organ. This method, therefore, gives results regarding digestion as such, and not of the amount of pepsin contained in the gastric juice. The conditions of the experiments are also those which determine the presence of inhibitory factors.

This principle of investigating the undiluted gastric juice may also be applied to other methods than the carmin test, *e. g.*, the refractometric method or the Mett tube method.

The Clinical Value of the Quantitative Methods for the Estimation of Pepsin

It is usually assumed that the pepsin secretion is of less diagnostic significance than that of hydrochloric acid, because it is less often disturbed. In view of Mett's method, as just described, however, this belief must be more critically tested, since it may be due to the fact that the earlier methods of pepsin estimation were faulty.

Pepsin and pepsinogen may be entirely absent, but then usually only in grave stomach disorders, especially in atrophic gastric catarrh, in carcinoma of the stomach, and in certain types of pernicious anemia. It is a very unfavorable prognostic sign, so far as the possibility of restoring the gastric function is concerned.

Examination of the Gastric Juice for Rennin and Rennin Zymogen

Normal gastric juice contains, besides hydrochloric acid and pepsin, rennin ferment and rennin zymogen as additional secretory products of the mucous membrane. In man and the pig the ferment is parachymosin, which is different in properties from the ferment chymosin found in the stomach of the calf. As we well know, rennin possesses the property of coagulating milk, independently of the help of acid.[1] Rennin zymogen, inactive in itself, is converted into rennin by acids. Rennin is rapidly destroyed by alkalis, but the zymogen is much more resistant to them.

To demonstrate rennin, 3 to 5 drops of gastric juice are added to 5 to 10 cc. of fresh uncooked neutral or amphoteric milk, and the mixture is placed in an incubator. If the rennin be present in normal amounts, curdling should take place in from ten to fifteen minutes (Leo). In this process the slight amount of acid added in the gastric juice will cause no precipitation. If the curdling take place very slowly, it is questionable whether it is due to the action of the rennin or to the formation of lactic acid, and so, to be exact, the reaction of the mixture

[1] This process, in which insoluble casein is formed from the caseinogen of the milk by the simultaneous action of rennin ferment and calcium salts, must not be confounded with the precipitation of unchanged caseinogen by acids (the curdling of milk by lactic-acid fermentation).

is taken before and after curdling has taken place. Rennin action is sure to have occurred only when curdling occurs without any change in the reaction.

Regarding the presence and the tests for the coagulating zymogen, the literature contains many statements of questionable value. According to Boas, it may be detected by making the gastric juice slightly alkaline with lime-water, and adding to it an equal volume of unboiled milk. If the mixture be placed in a thermostat, a dense coagulum will be formed in eleven to fifteen minutes. This test is not conclusive, for Fuld has shown that the zymogen is not transformed into the enzyme by salts of calcium, hence Boas' test depends simply on the action of small quantities of enzyme which are present being rendered more active in the presence of calcium salts.

Blum and Fuld have observed the presence of the zymogen of rennin only in gastric contents containing no hydrochloric acid, as otherwise the whole of the zymogen is transformed into the ferment. In order to test a gastric juice for the zymogen, one must make the juice acid with hydrochloric acid, allow it to stand for some time, and then test its coagulating activity. Before the gastric contents are tested for coagulating properties, the acid added must be neutralized with lime-water. A control test is made with the gastric juice which has not been treated with hydrochloric acid.

An approximate estimation of the amount of rennin in the gastric juice may be made, according to Boas, by not taking into account the time which is taken for coagulation, but by determining the least amount of the gastric juice which is necessary to coagulate a definite amount of milk. An increasing dilution of the gastric juice is added to equal volumes of milk, and the mixtures observed for the occurrence of coagulation. In normal gastric contents, a few drops of a dilution of 1 : 100 will suffice, while in severe cases of insufficiency, the dilution necessary may be 1 : 5 or 1 : 10.

The significance of these tests is similar to the estimation of pepsin, for in the gastric contents the secretion of pepsin and rennin are usually parallel, although it is assumed, following Hammarsten's observations, that the two ferments are not identical. The approximate estimation of the rennin has, therefore, the advantage over that of pepsin, that it is easier to perform. A total absence of the ferment is to be observed only in severe pathologic conditions of the gastric mucosa. According to Boas, the limit of dilution is of considerable diagnostic importance. Total absence of the ferment is found only in severe cases of gastric catarrh, gastric carcinoma, and in a group of cases of pernicious anemia.

Quantitative Estimations of the Coagulating Ferment, According to Blum and Fuld.—A preliminary test is made by adding to portions of 45 cc. of milk, 0.5 cc. of the filtered gastric juice, and increasing dilutions of the same. The mixtures are allowed to remain at 15° C. for two hours, and are then placed in a water-bath heated to 37° for five minutes. The more dilute the solution of the gastric juice is, which has been effective, the greater the concentration of the rennin. Blum and Fuld express this in terms of the dilution. A solution of gastric juice which still coagulates in dilutions of 1 : 8000 has a rennin value of 8000. Although the rennin value of the gastric juice may be very high, in antacid gastric juices one very often finds absolutely no ferment action.

Quantitative Estimation of Rennin According to Volhard.—Unboiled fresh milk is mixed with a few drops of oil of mustard for a preservative. Shortly before the test 2 cc. of normal hydrochloric acid are added to every 100 cc. of milk, and the mixture shaken in order to make the reaction of the milk suitably acid for coagulation. This small amount of acid does not precipitate the casein. The gastric juice is diluted 1 : 10 and 1 : 100. The first is called dilution I, the second dilution II. Three rows of test-tubes (9 in each row) are labeled as follows:

0.9, 0.8, etc., to 0.1 (pure gastric juice).
0.9, 0.8, etc., to 0.1 (dilution 1 : 10).
0.9, 0.8, etc., to 0.1 (dilution 1 : 100).

The test-tubes are then filled with the corresponding amounts of gastric juice, and into each test-tube is poured 10 cc. of cold HCl-milk, the mixture is shaken, and after the tubes have stood for one hour in cold water or in an ice-chest, they are placed in a thermostat at 40°. In this way the change of casein into paracasein takes place at a low temperature. The secondary coagulation of the paracasein, by its combination with salts of calcium, whereby a paracasein-calcium compound is formed, takes place at once on warming the solution. On examination, all the more concentrated solutions will be found coagulated up to a certain point; the rest will remain liquid. With normal gastric contents, which give an acid reaction with Congo-red paper, the boundary will be found in the second group of test-tubes. With achylic

contents, the highest concentration of gastric juice will sometimes be found ineffective. In most cases, where with ordinary methods no coagulation is obtained, one still finds the test positive in the higher concentrations. If one does not wish to go to the trouble of preparing three sets of test-tubes, one may make a preliminary test with 0.1 and 0.01 cc. of the undiluted juice. This will show whether one should use a 1 : 10 dilution or 1 : 100.

As in the method of Blum and Fuld, one may express the results by the relation between the amount of gastric juice and the amount of milk used in the tube containing the smallest amount of the former sufficient for coagulation.

Estimation of the Fat-splitting Action of the Stomach-contents According to Volhard.—The fat-splitting action of the stomach-contents, which at one time, following the investigations of Marcet, Cash, Ogata, and Scheuerlen was thought to be due to bacterial action has been reinvestigated by Volhard. It has now been proved beyond question to be due to a lipase or steapsin.[1] This action is not inconsiderable, and has physiologic value. It follows the Schütz-Huppert law with regard to time and concentration, in which the degree of activity is proportional to the square root of the time of reaction and the amount of ferment. Volhard and Stade[2] have worked out a simple quantitative method for the estimation of the fat-splitting activity. The method which has been given by Riegel[3] is as follows:

The yolk of one egg is diluted with 30 to 40 cc. of water, and to 10 cc. of this mixture a measured amount of the gastric juice is added after both have been previously heated to body temperature. The mixture is allowed to stand a certain time at this temperature. It is then cooled, placed in a separating funnel, and shaken out with 75 cc. of ether containing a few cubic centimeters of alcohol. A measured portion of the ether is transferred to a beaker, and 50 cc. of neutral alcohol are added. Phenolphthalein is then added, and the mixture titrated with decinormal alkali to a faint pink. To this mixture is then added 10 cc. of normal sodium hydroxid, and heated with a reflux condenser on the water-bath for two hours, using a soda-lime tube to protect the mixture from the carbon dioxid of the air. The flask may also be allowed to remain at room temperature for twenty-four hours. In this way one completes the saponification of the neutral fat. Ten cc. of normal acid are then added, whereby the fatty acids are set free. A second titration with decinormal alkali will give the amount of fatty acids which has not been formed by ferment action. From this, one may estimate the percentage of fat which has been split by the lipase in the gastric juice. The square of this number divided by the time of digestion gives the number of units of ferment contained in the gastric juice.

In cases of hypochylia and achylia, the amount of fat-splitting action is decreased up to total absence.

The butyrometric method may also be employed for determining the degree of fat-splitting. (See p. 487.) This is given from the difference between the acidity of the filtered and unfiltered contents of the stomach, after subtracting the acidity of the soup itself. In order to do this, the contents of the stomach must be boiled immediately after siphonage, in order to stop the further action of the ferment outside the body.

Examination of the Mucous Secretion of the Stomach

The gastric juice always contains mucus (mucin), in the form of more or less tough, transparent or cloudy flakes. If conditions be normal, these mucous flakes are always very small. They are easily stirred up in the rinse water. Swallowed mucus from the pharynx, esophagus, or bronchi is generally distinctive. It usually occurs in larger isolated lumps, and contains more pus-corpuscles than the mucus from the stomach. If it be foamy or pigmented (lung pigment), and if it contains no food-particles, which are so often intimately mixed with stomach mucus, the distinction is usually easy. The microscope will often solve the origin of the mucous constituents, for frequently in the interior of the mucous flakes a characteristic type of epithelium may be found, *e. g.*, pigmented lung epithelium. True stomach mucus, if the digestion be good, contains only the nuclei of large round or oblong epithelium cells and of leukocytes, because the cell plasma has been destroyed by the digestion. If the digestion be impaired, we can often see the cells of the stomach epithelium *in toto*. An increase in the amount of mucus, with an abundance of the polymorphous nuclei of leukocytes, is characteristic of gastric catarrh. We must be very cautious before assuming the presence of an increased

[1] Zeit. f. klin. Med., vol. lii and liii.
[2] Stade, Inaug. Diss., Giessen, and Hofmeister's Beiträge, 1903, 3.
[3] Erkrankungen des Magens in Nothnagel's spec. Pathologie, 1908, second ed.

mucous *production*, for an abundant mixture of mucus in the stomach-contents quite as frequently depends upon a diminished solution of the mucus in consequence of a diminished production of HCl. Besides, we must remember that the mucus swells considerably if free hydrochloric acid be absent, and so the amount may seem increased. For this reason very noticeable amounts of mucus are found with carcinoma of the stomach. We may finally mention that a quantitative estimation of mucus, which is so frequently advocated, is usually impossible by chemical means. The mucus cannot be precipitated in the filtrate of a test-breakfast, because the mucin which is dissolved in a gastric juice that contains hydrochloric acid, or that which is even partly digested, can no longer be precipitated by acetic acid.[1]

The view that mucus is not digestible has been changed by modern investigations.

Salomon's Test for the Contents of the Fasting Stomach, and its Use in the Early Diagnosis of Carcinoma of the Stomach

Salomon has shown that in conditions where there is an ulcerated surface of the stomach due to a new-growth, considerable quantities of proteins are to be found in the exudate from the ulcer; and that a large content of protein in the siphonage from the fasting stomach may be used as a sign of a new growth in the organ. The stomach is thoroughly cleaned out by lavage with water the evening before the test is made, and in the morning 400 cc. of physiologic salt solution are poured into the stomach, and by repeatedly raising and lowering the siphon the stomach is thoroughly washed with the solution. Salomon estimates the amount of albumin in the wash-water by Esbach's method, or the nitrogen content of the fluid may be ascertained by a Kjeldahl nitrogen determination. Salomon suspects carcinoma of the stomach if he obtain a well-marked flocculent precipitate after the addition of Esbach's reagent, or if the amount of nitrogen in 100 cc. of the fluid exceed 20 to 25 milligrams.

Reicher[2] has shown that in Salomon's test the greater part of the protein is nucleoalbumin. He believes that Salomon's test shows the increased cell destruction at the surface of the ulcer. Reicher suggests, in order to avoid the complication of much mucus, to make a control test by adding a little acetic acid. J. Witte[3] has shown that in the investigation of six cases of authentic carcinoma of the stomach the nitrogen content did not exceed 20.3 mg. per 100 cc., and in no case did the Esbach value exceed $\frac{1}{2}$ per thousand. He concludes that Salomon's test is not positive even in those cases where both in the contents of the stomach and in the stool, blood may be detected without difficulty.

Examination of Gastric Contents for the Products of Protein Digestion

Although it would seem valuable and practical to obtain some insight into the digestive functions of the stomach from an analysis of the chemical changes that the various foods undergo during digestion, yet experience has proved this is not feasible. The processes are too complicated, for the changes from proteins to albumoses and peptones depend not only upon chemical reactions, but also to a high degree upon the power of absorption and of motility of the stomach. Because a test-meal is rich in albumoses, for instance, we cannot conclude that the digestion is especially good, but rather the contrary, because the albumoses formed are normally either quickly absorbed or passed on into the intestine. An abundance of protein, therefore, or an increase in the amount of peptone contained in the stomach-contents, would indicate, generally speaking, disturbed gastric digestion. But any such deductions could be based only upon an accurate quantitative determination of the proteins of the stomach-contents, and as yet we possess no available clinical methods for such a determination.[4]

[1] Compare A. Schmidt, Ueber die Schleimabsonderung im Magen, Deut. Arch. f. klin. Med., 1896, vol. lvii, parts 1 and 2, p. 65.

[2] Arch. f. Verdauungskrankheiten, vol. vii.

[3] Zeit. f. klin. Med., lxv, No. 1 and 2.

[4] This subject is treated in Neumeister's Text-book of Physiologic Chemistry.

Bacteriologic Examination of the Stomach-contents

With added experience the author has come to the view that a large group of gastric disturbances is due to bacterial infection, a view which has been at variance with the conceptions regarding the antiseptic power of the gastric juice. How insufficient this antiseptic power is to prevent a profuse growth of bacteria is seen in cases of gastric stasis, in which condition no doubt exists as to the part which the micro-organisms play.

In cases of disturbance of the motility of the organ where the growth has been overlooked through exclusive attention to the test-breakfast, bacteria are a very important factor. This is due to the fact that examination of the stomach after the usual meal shows interference with motility, and partly that while the antiseptic power of the gastric juice is not entirely lost, the epithelium of the stomach-wall, when once damaged, takes part in the process only to a very small degree.

While the author previously recommended the bacteriologic investigation of the contents of the stomach after the flour-soup test-meal, he is now inclined to lay greater stress on the washings of the fasting stomach. One finds in this fluid the bacteria which have been swallowed with the saliva, but the appearance of large numbers of these, and the predominance of certain forms, especially after culture, has a very distinct diagnostic importance. Regarding the pathogenic quality of the micro-organisms, we are insufficiently orientated, but it is hoped that a careful study in this direction will yield results of very distinct value. Severe bacterial disturbances may be recognized from an examination of the vomit. (See p. 428.)

The Bacteriology of Gastric Carcinoma.—This is of especial value in the early diagnosis of cancer of the stomach. The frequent occurrence of the Boas-Oppler bacillus in the antacid or hypoacid contents of the stomach is characteristic. It is shown in Fig. 201 and is described on p. 430. This micro-organism has been called by Palier Bacillus geniculatus,[1] from the fact that two of the organisms bent at the end are found in close proximity to one another. The bacillus is non-motile, is 6 to 8 μ long, and is Gram positive. It often grows in chains. It is probably the most important lactic acid former in the carcinomatous stomach. It grows best in a limited supply of air. It is best grown in deep stab cultures in glucose-agar, at 38°. The bacillus may be isolated, according to Palier, by digesting 2 cc. of boiled meat and 5 to 6 cc. of the gastric juice. As the hydrochloric acid disappears from the gastric juice, the bacillus grows with the formation of lactic acid. Palier regards as especially characteristic of gastric carcinoma that besides the Bacillus geniculatus, there are found streptococci and staphylococci, few yeast-cells, and no molds.

The Bacillus geniculatus is also found in decreased acidity of the stomach without the presence of a malignant growth, so that one cannot assign to it, as was previously supposed, a distinct pathognomonic importance. It is, however, most suspicious when the organism persists in spite of frequent gastric lavage, and when the stomach does not present the signs of insufficient motility. In these cases there must be pockets in the stomach in which the organism lodges, and these are seen in organs affected with a malignant growth. It must, however, be pointed out that mistakes may be made even here. The author diagnosed a case as gastric carcinoma from the finding of the organism, and a metastatic recurrence of the same in the mucosa. The section showed that a metastasis had formed, but not in the mucosa. This was perfectly intact. A pocket was present in the stomach, due to operation in consequence of a gastro-enterostomy. In the pyloric end of the stomach was a pocket in which the bacilli were found in large numbers.

Examination of the Stomach-contents for Gas Fermentation

The fermentative processes which take place in the stomach when the digestion is affected, especially if there be also a motor insufficiency, have been studied recently, partly by bacteriologic examination and partly by chemical analysis of the gases which develop in the fermenting gastric contents, *i. e.*, in the expressed test-breakfast. These examinations as yet have been productive of no practical results. The existence of fermentation can be demonstrated by placing some of the gastric contents in a fermentation tube (like the one used for estimating sugar in the urine) and letting it stand in an incubator (Fig. 238). If gas forms, it will accumulate above the fluid. If we wish to examine it more closely, we can collect the gas formed from a considerable amount of the stomach-contents in a larger vessel by conducting it through a tube and a pneumatic trough into an inverted tube filled with mercury.

[1] Sandberg, Zeit. f. klin. Med., vol. li, p. 80, and Palier, Presse Médicale, 1906.

The gases which are found most frequently in the gastric contents are carbon dioxid and marsh-gas, CH_4. The former is easily recognized by its characteristic of clouding baryta water, and the marsh-gas, by the peculiar flame with which it burns.

DIAGNOSTIC IMPORTANCE OF THE USE OF RIEGEL'S TEST-MEAL

Concerning the value of Riegel's test-meal, it is to be noted that, since from a motor as well as a chemical standpoint it makes greater demands upon the stomach than the Ewald test-breakfast, it at the same time acts as a greater stimulus to digestion, and consequently exhibits to better advantage existent anomalies. A stomach whose motility appears perfectly normal, as indicated by the test-breakfast, may, when tested with Riegel's meal, show itself decidedly insufficient in motility by not having completely emptied itself for hours afterward. By the use of this test-meal there are obtained two diametrically opposed results to those given by means of the test-breakfast. For example: a chemical insufficiency of the stomach (hyperacidity, lack of enzyme) may be made to appear more plainly by the use of the test-meal than by the breakfast; on the other hand, a hyperacidity or hypersecretion that has escaped notice in the test-breakfast may become manifest by the strong stimulation of secretion by the Riegel meal. From these facts it is evident that in stomach affections where the use of the test-breakfast does not lead to a clear interpretation, the examination is to be repeated by means of Riegel's test-meal.

Concerning the most advantageous time for the siphonage of the Riegel meal, see p. 444. There unfortunately still exist too few results for us to be able to calculate normal figures for the acid and enzyme contents of the stomach-contents, as well as for the volume of the fluid removed by siphonage, at various times after administration. As a rule, it will be found that after four hours the percentage acidity of the Riegel test-meal will correspond to that of the Ewald-Boas test-breakfast after one hour, and that after seven hours a normal stomach will have easily emptied itself of the Riegel meal.

DRY TEST-MEAL

The author, in the first edition of this work, pointed out the difficulties which are encountered in using the Ewald test-meal, and also that of Riegel in that it is impossible to say from the amount of fluid which has been siphoned off how much is due to the meal, and how much is the result of the secretion of the stomach. He has suggested that the fluid be left out of the test-meal, and that for this purpose a single roll be given. One can in this way obtain information regarding the amount and character of the secretion. Boas [1] has further suggested in this direction that five Albert biscuits be given instead of a roll. The idea is that bread contains water, which should be avoided. This is not altogether correct, for estimations of the moisture in ordinary bread have shown that the amount present does not play any important part. On the other hand, the use of Albert biscuits has the disadvantage that they cannot be swallowed without some mastication, whereby a not inconsiderable quantity of saliva will be secreted, which will be reckoned as gastric secretion. Bread which has not been baked too long will not have this disadvantage.

BOUILLON TEST-MEAL

Talma [2] recommends a test-meal consisting of 1000 cc. of a watery solution of Liebig's extract, 0.3 per cent., which has been neutralized with soda, and which is poured into the stomach with a stomach-tube. Talma bases his method on the investigations of Schiff and Herzen and of Pawlow, who have shown that Liebig's extract is exceptionally potent in promoting the secretion of gastric juice. In this form the method does not appear to the author to possess any especial advantage,

[1] Deut. med. Woch., 1907, No. 4. [2] Berlin. klin. Woch., 1895, No. 6.

as the neutralization and the administration by a tube are both unphysiologic. It has one advantage in that one is able to remove the contents of the stomach completely. Schalij[1] has proposed to make the acidity of the gastric test-meal up to 0.2 per cent. HCl, and after a time to remove the contents, and to estimate the acidity of the gastric contents. As water is not absorbed from the stomach, one can obtain information regarding an increase or decrease in the acidity. Naturally, such information is limited, as a small amount of gastric juice of high acidity will give the same results as a larger amount with a smaller content in acid. Moreover, the addition of hydrochloric acid to the test-meal is another unphysiologic procedure.

EXAMINATION OF THE FUNCTIONS OF THE STOMACH BY MEANS OF THE BUTYROMETRIC METHOD OF SAHLI AND SEILER

It can hardly escape the thoughtful reader how great must be the uncertainty attached to conclusions as to the functions of the stomach which are drawn from examinations of test-meals, even those in which the most exact chemical methods are employed. The main difficulty lies in the fact that the results of the quantitative examination of the stomach-contents are influenced by many different factors which do not allow of separate calculation. For example, the amount of the expressed meal is not entirely dependent upon the motility of the stomach, but is altered also by the quantity of the secretion. Again, the acidity or the percentage content does not represent directly the amount of the secretion, but is influenced to a great degree by the motor activity. For the acidity which is present indicates a very different secretory activity according to whether the expressed meal contains besides the secreted gastric juice a greater or less part of the ingested test-meal, or according to whether a greater or less part of the secretion has passed, before expression, through the pylorus. If the greater part of the test-meal has passed quickly into the intestine during the hour before the expression, then even a small secretion may apparently be normal or even hypernormal; and the reverse is also conceivable—namely, that even a normal secretion may present subnormal acidity, and perhaps even indicate a lack of free hydrochloric acid, in case the food which was introduced has passed only in small amounts into the intestine during the time of the observation. For the percentage content of free hydrochloric acid is influenced not only by the motility of the stomach, but also by the solution and absorption of the protein in that organ. It is, for example, clear that if the proteins be quickly absorbed, the excess of acid will appear much more quickly than if at the time of the examination all the proteins of the food have been saturated by the acid.

It must be emphasized that, if we determine the presence of a chemical abnormality in the gastric contents according to the older methods, it is not possible to say whether the disturbance is dependent upon the secretion or upon the motility or upon absorption, or upon all these three factors together. If, then, we consider this, it must be admitted that the experiments of Pawlow, who succeeded in collecting pure gastric juice free from the admixture of water and food, were the first to give us exact data concerning the laws of the secretion by the stomach.

From the preceding description of the usual methods of examination, in spite of the fact that even with the difficulties surrounding them certain results have been obtained which are of value from a therapeutic standpoint, it is evident the apparent accuracy of the results of these

[1] Review in Semaine médicale, 1908, No. 21.

methods as applied to the stomach is really a delusion, and that a part of the trouble which has been expended upon them must be considered as actually lost, since it has not been possible to differentiate in the results the separate factors mentioned above. We have to do with an equation containing several unknown quantities which cannot be solved so long as other equations are not at our disposal. Proceeding along similar lines, Pfaundler, in his very interesting work, has brought forth several equations for the chemical process of digestion, and so has found a method of getting more exact information regarding the secretion and motility of the stomach. The essentials of Pfaundler's method consist in removing, during the period of the digestion of the test-meal, portions of the stomach-contents at different times, either on the same day or with a repetition of the test-meal on different days. The analytic data obtained from the examination of these various portions have been used by Pfaundler to prepare equations from which he has been able to calculate, in absolute figures, the motor activity and the amount of the secretion of the stomach. But this method is entirely too complicated for practical purposes, and for the patient is much too troublesome; besides this, it is not entirely free from physiologic objections.

Principle of the New Method

In order to obviate, in part at least, the indefiniteness of our examination of the stomach, the author reasoned as follows: If it be possible to add to the test-meal a substance which is not easily absorbed and yet allows of ready quantitative determination, then after introduction and subsequent expression, from the amount of this substance present in siphonage it can be calculated how much of the test-meal has passed into the intestine, how much is still remaining in the stomach, and consequently what fraction of the expressed content can be ascribed to the secretion of gastric juice. One obtains, therefore, a measure not merely of the motor activity of the stomach, but also of the secretion as well. For the success of such a method it is evident that: first, the test-meal must be homogeneous throughout, and that in order to serve as an indicator of the motility the unabsorbed substance must remain thoroughly mixed in the stomach-contents, *e. g.*, present no inclination to separate or sediment; and, second, that absorption of water must not take place from the stomach. According to the experiments of von Mering, this latter fact may be considered as definitely settled. Concerning the choice of indicators for the motility of the stomach, the author thought first to add an insoluble colored powder or lycopodium to the test-meal, and to determine this quantitatively by colorimetric means or by counting the lycopodium granules. It was soon shown, however, that neither the insoluble colored particles nor the lycopodium was sufficiently well mixed throughout the test-meal to serve as a measure for the amount of the test-meal remaining in the stomach. The powders attached themselves so intimately to the solid particles of the test-meal that the experiment was abandoned. Moreover, there was still another point to be considered. The substances mixed with the test-meal must not give it the character of a non-physiologic food, even if this character consist merely in an abnormality of appearance or taste. On this account the writer was convinced that the only substance which appeared feasible for the purpose in question was fat.

The use of fat in test-meals essentially for the sole purpose of the determination of motility had previously been proposed by Matthieu.[1] He added to a test-meal consisting of 60 gm. of bread, 20 to 70 gm. of oil, in the form of an emulsion with gum, and 250 gm. of tea. He then obtained by means of the determination of fat data concerning the motility and secretion of the stomach, although the latter was merely incidental and was not carried out to any definite conclusion. The author does not know whether this method of Matthieu has been found to be practicable. In any case this test-meal did not appear to the author to be available for the point in question, because it did not fulfil the postulate of homogeneity, in that the pieces of bread exhibit a decided inclination to sediment, and thereby mechanically remove an unknown part of the fat. In consequence of this the fat, other food constituents, and the secreted juice do not allow of quantitative determination. Besides this, such a mixture of an emulsion of oil with the ordinary test-meal cannot be considered as a usual diet, nor on account of its unpleasant taste is it a test-meal of physiologic composition. The experiments of Pawlow show sufficiently how very easily the physical characteristics of the test-meal influence the functions of the stomach.

Again, v. Mering, in his method of proving the power of absorption of the stomach, employed fat in the form of an emulsion of the yolk of egg. T. Volhard, nevertheless, has shown that such emulsions of the yolk of egg are not permanent within the stomach; as a result of the influence of the hydrochloric acid, the egg-yolk separates, and the postulate of homogeneity is consequently not fulfilled.

The attempt was made next to use milk, since this presents a mixture of protein, carbohydrate, and finely divided fat, which is easily obtainable and nearly ideally constituted for the purposes of nutrition. The experiments with milk resulted unfavorably, in that the coagulation of this substance which took place in the stomach disarranged its homogeneous composition. It was easy to show that in the coagulation the fat was carried down almost completely by the precipitation, and that the coagulum and whey in the expressed test-meal of milk contained very different amounts of acid. We were not able by various artificial means to compel the milk to coagulate in fine flocks, and thus to avoid any considerable appearances of sedimentation in the stomach. The employment of milk was consequently also excluded.[2] Finally a soup made of flour browned in fat proved to be adequate for our purpose, and yet completely suitable for ordinary nutrition. At the author's suggestion, his assistant, Dr. Seiler, tested the feasibility of the employment of this test-meal for the purpose in hand, and made a number of examinations, which have been published in his dissertation.

Preliminaries of the Method

Preparation of the Flour Soup.—This can be very readily prepared by the physician immediately before the examination, and requires only a few minutes' time. The method is as follows: 25 gm. of flour and 15 gm. of butter are fried in an iron pan until well browned[3]; and about 350 cc. of water are then added gradually with constant stirring. The mixture is then boiled for five minutes, and the loss in volume replaced by fresh water. Salt (sodium chlorid) is now added to give the soup a pleasant flavor. The mixture must not contain any lumps. This soup presents a well-mixed emulsion of fat, which, probably because it is mechanically well mixed with the flour, remains

[1] Arch. f. Verdauungskrankh., 1896, vol. i.

[2] A further reason for abstaining from the use of milk was the fact that, in opposition to the results of Schüle (Zeit. f. klin. Med., vol. xxviii), the author was never able to detect free hydrochloric acid in an expressed test-meal of milk of 200 to 300 cc. This difference is attributable to the better quality (fat and protein content) of the cows' milk used in his laboratory.

[3] The flour may be fried beforehand and kept in tins in a cool place to prevent the melting of the fat. As the flour is sterilized by the process, the mixture keeps for a long time. In this way the procedure is simplified, as one has only to weigh out 35 gm. of the flour, and boil it with water in order to form the soup. In many instances the objection which has been raised to the method is based on the improper preparation of the soup. When once the method has found general application, which is only a matter of time, the flour will be prepared on a commercial scale, and be available at any time.

intact, in spite of the action of the acid in the stomach, and shows no inclination within the time of the examination to form a sediment or for the fat to separate.[1] In fact, at the end of the digestion such a flour soup is expressed in about the same physical condition as it was introduced. It is merely more or less diluted.

The patient takes with a spoon 300 cc. of this soup, while the remaining 50 cc. are retained for control determination of the content of fat. The stomach must have been thoroughly washed before administration, and after one hour the contents are expressed.

The next step to be taken is first to determine the absolute amount of fat remaining in the stomach after the test digestion, and, secondly, to compare this amount with that introduced. By the use of the special perforated stomach-tube (see p. 445) we are now able to express the contents of the stomach completely. The estimation of the amount remaining by the method of Matthieu[2] is now no longer necessary.

For the next step in the procedure it is necessary to have a clinical method for the *determination of the fat* in the fluids to be examined. The usual method, according to Soxhlet (extraction with ether), is too detailed and lengthy to be suited for clinical purposes. On the other hand, the author has found that Gerber's[3] butyrometric method for fat-determination, which is often employed in the examination of milk, answers all the demands of simplicity and exactness. He will, therefore, next describe this method of fat-determination, which has not been used before for clinical purposes. The principle is as follows: The solutions in which the fat is to be determined are mixed with a definite amount of concentrated sulphuric acid and a very small volume of amyl alcohol and thoroughly shaken; since the mixture becomes quite hot, the action of the sulphuric acid tends to decompose the organic substances,

[1] That sedimentation and separation do not take place even when the flour soup remains quietly in a glass is a further proof that even the slightest peristaltic movements of the stomach cause the homogeneous character of the meal to be maintained, and completely exclude any sedimentation which might be caused by the addition of the gastric juice.

[2] The principle of this method consists in the dilution of the residue in the stomach by means of a definite volume of water, which is introduced by means of a tube, and in the expression of the diluted stomach-contents after the water has been thoroughly mixed in the stomach by means of light kneading. The acidity of the undiluted, as well as of the diluted, stomach-contents is then determined by titration (p. 453), and from the differences in these two values conclusions may be drawn as to the degree of dilution; or, since the amount of water which was added is known, as to the residual amount of stomach-contents which was not expressed. The following is the method of calculation according to Matthieu:

Let a = acidity of the undiluted gastric contents.
Let b = acidity of the diluted gastric contents.
Let x = amount of the test-meal remaining in the stomach after expression.
Let 300 cc. = the amount of water introduced into the stomach for dilution.
Then $ax = b\,(x+300)$.

$$\therefore\ x\,(a-b) = 300\,b.$$

$$\therefore\ x = \frac{300\,b}{a-b}.$$

This method has proved unsatisfactory on account of the difficulty of mixing the water used for rinsing with the gastric contents; and because the author's method for completely emptying the stomach makes it superfluous. Rinsing with 300 cc. of water is used only as a control. It is shown that by using the procedure mentioned on p. 445, the rinse water is recovered almost perfectly clear, showing that the residue is absolutely negligible.

[3] Die praktische Milchprüfung, Bern, K. J. Wyss, 1900.

with the exception of the fat, to such an extent that a thin solution results; from this the total amount of fat dissolved in the amyl alcohol can be separated in the form of a clear layer by means of centrifugalization. The volume of fat-amyl-alcohol layer is then read off in a butyrometer specially constructed by Gerber. The readings on the graduated scale are calculated as fat per cent. by weight. The butyrometer, made of hard glass, is about 20 cm. long. Its shape may be seen from Fig. 209. The apparatus has the disadvantage that centrifugalization cannot be performed with the ordinary clinical centrifuge, which has too small a radius; this necessitates the employment either of a much larger centrifuge or of one designed especially for this purpose, such as can be obtained from Hugershof, in Leipzig. These centrifuges are very expensive, and when running at a high rate of speed, are exceedingly noisy.

In order to circumvent this disadvantage, and at the same time to be able to use a centrifuge, the author has had smaller tubes constructed which have half the volume of the original Gerber tubes. The measurements with these tubes are sufficiently accurate for clinical purposes. The tubes are capable of being used in the ordinary clinical centrifuge, if special rings to carry the holders are obtained with them. They may be had from the optician Büchi in Bern. By using a good clinical centrifuge, the separation of the fat is complete in two minutes. With this method, both the use of the original large tubes and the more time-consuming heating method, which will be mentioned later, are completely superseded.

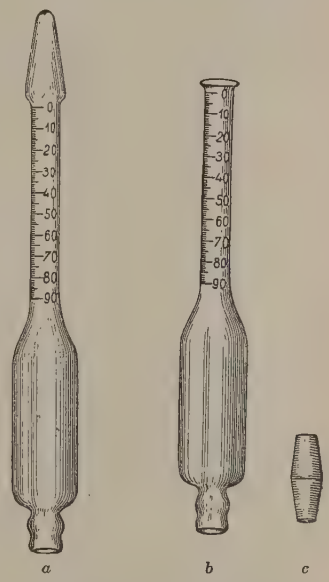


Fig. 209.—*a*, Original butyrometer for the centrifuge; *b*, open butyrometer for boiling method; *c*, double-coned rubber stopper.

The heating method is described for those clinicians who do not possess a centrifuge. This method depends on the fact that if a mixture containing fat be heated for ten minutes with amyl alcohol and sulphuric acid, the fat rises to the top and can be measured off. For this purpose the ordinary butyrometer cannot be used. A special form must be employed, shown in Fig. 209, b, in which the smaller end is open.

The butyrometer is filled by means of pipets, also especially designed for the purpose. Of these are required a 10 cc. (for the sulphuric acid), a 1 cc. (for the amyl alcohol), and an 11 cc. (for the milk, the flour soup, or stomach-contents).

The author must here make reference to the *presence of a lipolytic enzyme in the gastric juice*, which has been of late carefully studied by F. Volhard.[1] The thought presents itself that perhaps in an examination of the digested stomach-contents, since a part of the digested fat

[1] Münch. med. Woch., 1900, parts 5 and 6; Zeit. f. klin. Med., vol. xlii and xliii.

may have been split in the stomach, the amount of fat after siphonage cannot serve as an indicator for the amount of the residual test-meal. The separated glycerin and butyric acid (if butter-fat be employed) are both soluble in water, and, if they are not absorbed by the stomach, consequently remain in the watery, instead of in the alcoholic, layer, and thus escape estimation. The action of the enzyme in this connection was studied by the author's assistant, Dr. Seiler, and his results, published in the Archiv für klinische Medizin (1904–05), show that the amount of fat decomposed is so slight that it may practically be neglected. The flour soup is expressed after one hour, and Seiler has shown that the lipolysis in this length of time is inconsiderable. Furthermore, almost all of the fatty acids contained in butter-fat are insoluble in water, so that they pass almost entirely into the alcoholic layer of the butyrometer. The butyric acid, which is soluble in water, is present in such exceedingly small quantities that it may be disregarded. Owing to the relatively small amount of glycerin contained in the fat, it follows that even if there be considerable lipolysis, the loss in the alcoholic layer due to the solution of the glycerin in water is so slight that it is practically unimportant. In other words, the fatty acids liberated by lipolysis in butyrometry may be read off as fat, and the result will be fairly accurate.

Although lipolysis does not interfere with the butyrometric determination, Volhard has shown that if the hydrochloric acid of the gastric juice be small in amount, the acidity due to the liberation of the fatty acids by lipolysis may markedly influence the total acidity; it would consequently be incorrect to refer this total acidity entirely to hydrochloric acid. The simplest method for avoiding this error is to employ the filtered gastric contents for the titration of the acidity. With the exception of the quantitatively unimportant butyric acid, the fatty acids are insoluble in water, and so, since they remain upon the filter, the acidity of the filtrate may be referred directly to hydrochloric acid.

It is also to be remarked that it is advisable to determine the amount of fat in the undigested flour soup, as well as the amount in the expressed meal. This can be done without any especial trouble. This is particularly advisable because, on account of the varying content of water in butter, we cannot, by weighing the amount of butter put into the soup, assume the weight of the fat-content.

Next follow the technical conditions which must be insured in the use of Matthieu's determination of the residue contents and Gerber's butyrometric fat-determination in order to be able to draw exact conclusions concerning gastric digestion.

The process is as follows: 5 cc. of sulphuric acid (specific gravity 1.820 to 1.825 at 15° C.) (corresponding to 90 to 91 per cent. acid) are added to the small butyrometer by means of the pipet, and upon this is stratified 0.5 cc. of pure amyl alcohol (specific gravity 0.815 at 15° C.), and then 5.5 cc. of the flour soup or stomach-contents. The butyrometer is then carefully closed by means of a rubber stopper, and thoroughly shaken. On account of the heat the tube must be covered with a cloth. It is finally centrifugalized, during which process the graduated end of the butyrometer must lie toward the center. By the centrifugalization the fat and alcohol separate from the mixture, and lie as a clear, transparent layer on top of the solution, which is now darkly colored. Centrifugalization is carried on as long as the height of the

alcoholic layer increases. In case the operation is not undertaken immediately, the butyrometer must be placed in water at a temperature of at least 70° C., in order to prevent the hardening of the fat. In order to obtain exact results the reading should be made while the fluid is still warm. For the purpose of reading, the rubber stopper must be pushed into the mouth of the butyrometer so that the upper surface of the layer of fat (with its under meniscus) comes to lie at the zero-point of the scale.[1] The scale (empirically graduated) is then read off at the point corresponding to the lower meniscus of the fat-layer. The centrifugalization should be repeated, particularly by those who are inexperienced in the method, in order to insure the accuracy of the estimation. If the estimation be correct, the second centrifugalization must give exactly the same reading as the first. Gerber found that this method for the determination of fat is exact for milk to about 0.1 per cent. Control experiments which were undertaken at the author's suggestion, in order to compare the results from this instrument with those from the Soxhlet apparatus, have shown that this degree of accuracy holds good for the flour soup before and after the action of stomach digestion.

Method of Fat Estimation Without the Use of a Centrifuge.—The open butyrometer is filled (Fig. 209, b) by closing the smaller end with a cork, and placing it in a test-tube rack with the larger end upward. After the flour soup has been warmed and thoroughly mixed by shaking, 10 cc. of the soup are poured in, and 1 cc. of amyl alcohol and 10 cc. of sulphuric acid added by allowing them to flow down the side of the tube in order to form a layer. The larger end is now closed with the rubber stopper. As the contents of the tube become warm it is necessary to hold both stoppers firmly with the hand. It is, however, wise to inclose the tube in a towel, in case it should break with the heat evolved. This rarely happens. The tube is then shaken, both stoppers being firmly held by the fingers. As soon as the mixture is complete, the upper, smaller stopper is removed. The tube is then placed in a boiling water-bath, adjusting the lower stopper so that the fluid is not high in the neck. From time to time the stopper is so adjusted that the layer of fat which is formed is just under the neck. The butyrometer is not placed directly on the bottom of the water-bath, as the formation of bubbles disturbs the tube and prevents the formation of fat as a homogeneous layer. Several tubes may be charged at the same time. After the butyrometer has remained for ten minutes at boiling temperature, the foam which is at first formed disappears, and the first reading may be made. In order to do this, the butyrometer is taken out of the water-bath and, being held in a slanting position, the lower stopper is so adjusted that the layer of fat rises within the limits of the scale. This must be done carefully else small particles of other substances than fat will be included in the layer. As soon as the fat is in the proper position, the tube is held vertically and the amount of fat read off. Each division corresponds to 0.1 per cent. fat. It is not necessary to adjust the fat layer to zero: it is only requisite to read the difference between the upper and lower divisions. With practice one obtains a perfectly sharp separation of the fat from the aqueous layer. In cooling, the layer of fat contracts, so that the reading must be made as rapidly as possible. The separation is not so well marked as by the use of the centrifuge, but the clear layer is sufficiently well defined. As a consequence of the longer heating of the flour soup with the acid there is much more carbonization. This does not, however, interfere in the least with the reading. If the separation be not perfect, the attempt may be made again by gently reversing the tube, and also by placing it again in the water-bath. In any event it is advisable to reverse the tube, in order to obtain a control of the reading. The larger value is always the correct one. One

[1] In centrifugalizing it will be found more practical to introduce the rubber cork so that the upper level of the fluid reaches only to about the 80 mark of the butyrometer scale, since the fat accumulates most readily in the conic part between the neck and the body of the butyrometer. By observing this precaution, moreover, the disturbing layer of insoluble substances (cellulose, etc.) collecting below the fat may be kept back in the wide portion of the butyrometer by cautiously bringing the instrument into the vertical position when the rubber cork is pushed in.

should also repeat the heating and read the level in the tube anew. This should be done until constant values are obtained. The estimation of fat takes, as a rule, about fifteen minutes. It may be objected to the method that, on heating, a part of the amyl alcohol is volatilized, and makes the scale of the butyrometer inaccurate. As, however, the boiling-point of amyl alcohol is 131°, this cannot be the case. Control estimations with the Soxhlet method have proved the accuracy of the method.

The stoppers which are used to close the butyrometers should be kept under water. In this way the rubber remains soft. This is absolutely necessary in order to obtain a perfect layer of fat. Before the butyrometers are used it is essential to try the stoppers to ascertain whether they fit the necks of the instruments perfectly. As vapor tension does not occur in the open instruments, it is not necessary to have the stopper fit so tightly. The stoppers may be dusted with talcum powder.

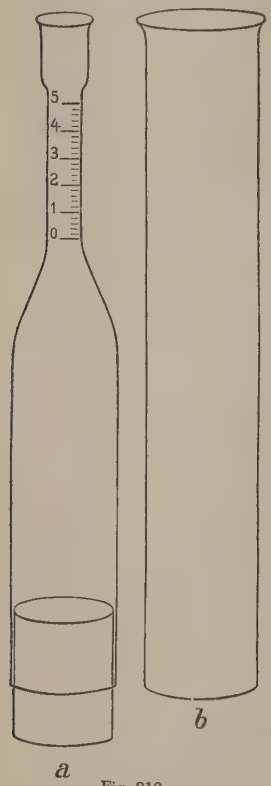


Fig. 210.

It may be mentioned that the small butyrometer for use with an ordinary centrifuge has been given the following form. (See Fig. 210.) This form has the advantage that the tube, open at both ends, which was originally designed for the boiling method, has been adapted for use with the centrifuge. It also has the advantage of avoiding any increase in vapor pressure, and of allowing the zero-point on the scale to be reached without any difficulty. The small neck (Fig. 209) at the lower part of the tube has been dispensed with, so that the larger stopper which is used gives greater latitude in adjusting the layer of fat. A larger purchase is also secured in adjusting the stopper. The tube is filled from the lower end, the neck being inverted and closed with a small rubber stopper. In centrifuging the mixture one should be sure to perform the operation as soon as possible after the gastric contents have been mixed with the sulphuric acid, and while the mixture is still quite hot. If the centrifuging must be delayed, the tube must be previously warmed to 70° before whirling. Centrifuging takes place with great facility in the smaller tubes, because the small mass of cellulose which is formed does not occlude the neck of the flask, as sometimes happens in the larger tubes. This is especially the case if the mixture is centrifuged while sufficiently hot. The cellulose with the coagulated proteins makes a mass larger in diameter than the neck of the tube. This is further facilitated by not allowing the fluid during centrifuging to rise into the neck. This may be done by a proper adjustment of the lower stopper. The mixture of acid and gastric contents should not be shaken too violently while mixing. With a good hand or electric centrifuge the operation is ended in three minutes, so that the method, in so far as rapidity and accuracy are concerned, leaves nothing to be desired. As the theoretic objections to the method have been explained away, the method deserves a wide application. While the makers of the tubes have been impressed with the importance of an accurate graduation, it is advisable to control new tubes after they are purchased. Although the scale should be absolutely correct, for the purposes of the butyrometric estimation it is only necessary that two tubes should correspond with one another. As the value for the total soup taken is divided by the value for the amount remaining in the stomach, the relative value is the important point, and therefore two tubes need only to correspond with one another to give accurate values for the butyrometric test. To assure one's self of this, the following method may be employed: Both butyrometers are closed at the lower end with their stoppers, and both are filled with mercury to the lowest mark. One of the tubes is then filled to the upper mark with mercury. With a fine pipet the mercury is removed from this tube and transferred to the other. In case the two tubes are equal, the mercury should lie between the same graduations in the second tube as it did in the first.

Fig. 210 shows a cylindric aluminum shield which is used with these tubes and takes the place of the conic shields ordinarily used in the centrifuge. These are supplied by the makers of the butyrometer tubes.

Performance of the Method

After a thorough rinsing of the stomach the patient is given in the morning 300 gm. of flour soup, prepared according to the method already described.[1] The remaining 50 cc. are retained for the determination of fat. After one hour the contents are expressed, as described on p. 444. A rest estimation, as was previously recommended, is completely unnecessary, as nothing remains in the stomach. The organ may be washed out with 300 cc. of water. If the siphonage has been properly carried out, the washings should contain but traces of the flour soup. Next, the amount of fat in the undiluted stomach-contents, and also in that portion of the soup which was retained as a control, is determined butyrometrically according to the method given above. The undiluted stomach-contents still remaining can be used for whatever qualitative or quantitative determinations may be deemed advisable. Qualitative examinations in this case normally show the same results as in the use of the ordinary test-meal. Free hydrochloric acid should be present; lactic acid should not. The flour-soup meal is very well suited for the determination of the pathologic formation of lactic acid, because it is free from this substance. In order to eliminate the fatty acids, the titrations are carried out with the filtered gastric contents. If titrations are also carried out with the unfiltered soup to which a quantity of alcohol has been added, the difference in the two titrations will give the amount of fat-splitting which has been performed by the gastric juice. In order to obtain comparable results, the same amount of alcohol must be added to both. A correction must also be made for the acidity of the flour soup itself. This, according to Seiler, is equal to 0.2 to 0.3 cc. of decinormal alkali. Seiler has shown that the soup contains a small amount of free fatty acids. The titration must be carried out immediately after the siphonage, as the fat-splitting may precede after the contents of the stomach have been removed. This may be avoided by boiling the contents immediately after removal. (See Seiler, Deut. Arch. f. klin. Med., lxxii). Besides the total acidity, the excess or deficit of acid may also be titrated. If the qualitative reaction shows considerable amounts of lactic acid, the determination of the hydrochloric acid must be made by Lütke-Martius' method, or that of the hydrochloric acid and the organic acids by Hehner-Maly's. Of course, all other advisable examinations can also be made upon the expressed gastric contents—namely, the qualitative and quantitative tests for pepsin and rennin (pp. 465 and 473) and the ordinary tests for starch digestion (p. 448).

[1] The author recommended originally that the soup be eaten with a spoon. As it appears that a considerable quantity of saliva is swallowed in this way, it may be better to allow the patient to drink the flour soup. This may be an advantage over the other test-meals. The author is not altogether in agreement with this view, as he looks upon the saliva as a necessary ingredient of the gastric contents. If it be conceded that the amount and acidity of the gastric contents in the butyrometric method are influenced by the saliva, in a case where the gastric contents are copious and the amount of acid small, a second test may be made by allowing the patient to drink the soup.

Calculation of the Results

The following calculations are possible from a consideration of the residue, from the acidity of the gastric filtrate, and from the difference between the amount of the fat found in the ingested flour soup and that found in the expressed contents.

We measure the amount of the gastric contents. As the siphonage has been complete, we designate this as *To* (total gastric contents after one hour). From the absolute fat-content of *To* found butyrometrically there can be determined how much of the volume *To* can be ascribed to the ingested flour soup, provided the expressed contents present a thoroughly mixed emulsion whose homogeneity has suffered no disturbance. Since the results of von Mering's investigations prove that absorption of water from the stomach is slight,[1] and since the absorption of fat in the stomach may also be neglected, the percentage relation of the fat to the stomach-contents is disturbed neither by the motility of the stomach nor by the absorption of water, but only by the secretion of gastric juice. The amount of fat remaining in the stomach serves, therefore, as a measure for the amount of flour soup also remaining; for example, if 300 cc. of flour soup, with a content of 4 per cent. fat, or altogether 12 gm. of fat, were introduced into the stomach, and the determination of fat for *To* showed a fat-content of 3 gm., we can conclude that the amount of ingested soup which remained at the end of the period was equal to $\frac{3}{12} \times 300 = \frac{1}{4} \times 300$—*i. e.*, 75 cc. We designate this amount as *Su* (soup).

Since we can neglect the absorption of water and the amount of the saliva which was swallowed, the volume *To* — *Su* is equivalent to the volume of gastric juice present in the expressed contents. This we designate as *Ma* (gastric juice). For example, if the amount *To* = 150 cc., and the amount *Su* = 75 cc., then 150 — 75, or 75 cc., will be the volume of gastric juice contained in *To*. If the acid content of *To* has been determined, it is possible from these data to proceed further, and to calculate what acidity was possessed by the pure gastric juice as it was secreted from the mucous lining of the stomach.[2]

If 75 cc. of pure gastric juice are present in the stomach-contents whose volume amounts to 150 cc., with 2 per cent. acidity, then the acid content of the pure gastric juice (*Ma*) must evidently be 4 per thousand. In a similar way the enzyme content of the pure gastric juice can be calculated if it has been quantitatively determined for the mixed stomach-contents.

In order to avoid misunderstandings in regard to the value of all these calculations, attention must be called to the following points:

Naturally, the volume *Ma* is not identical with the total volume of

[1] The fat-splitting of the soup which may occur within the hour is small. (See p. 484.) The amount of water-soluble substances, such as glycerol and butyric acid, which can be absorbed from the stomach is also minimal.

[2] In this conception of secretion there is an osmotic transudation of water, which may be excited by the flour-soup test-meal. As the content of the flour soup in water-soluble carbohydrates and salts is small, such an osmotic action should take place only in stomachs with disturbed resorption. The saliva must also be taken into account here, and where the estimation shows an abnormally low acidity, or a very large amount of gastric juice, one must be prepared to reckon with a dilution of the contents with saliva. In such cases the experiments may be repeated by the patient drinking the soup. In this way, less saliva will be secreted. (See foot-note, p. 487.)

gastric juice which has been secreted up to the time of expression. An unknown amount of the gastric juice mixed with the food has been passed on into the duodenum before expression. Nevertheless, the calculation gives interesting results as to the volume of the secretion independent of the percentage acidity of the pure gastric juice, since it shows us the relation of the amount of the gastric juice present in the stomach at a given time to the amount of test-meal present in the stomach at the same time. As later examples will show, this relation is approximately constant under normal conditions. The gastric juice and flour soup are contained in the volume To in approximately equal parts. From this it is evident that variations in this relation are of pathologic and diagnostic interest.

Concerning the conclusions as to the motility of the stomach which may be drawn from these results, the following is to be noted: The difference between the volume of soup introduced and that recovered by expression (namely, the volume $300 - Su$) can be considered as a measure of the motility of the stomach. Really this value does not correspond to the total motor power of the stomach, for an unknown amount of secreted gastric juice has also been passed on into the duodenum. At the same time it is probably a more reliable measure of stomach motility than the value of the total stomach-contents, which is used in the older methods for the same purpose. For, as already mentioned, the expressed contents contain under normal conditions about equal amounts of soup and gastric juice, so that it is easy to judge, when variations from this normal occur, whether a hypersecretion or diminished secretion is present. This gives the actual value of the motility already mentioned.

The calculations from the results of the examination can be presented algebraically as follows:

Let To = the amount of the expressed contents.
F = the fat-content of the flour soup in per cent.
f = the fat-content of the expressed contents in per cent.
Su = the amount of soup contained in the expressed contents.

$$\text{Then, } \frac{Su}{To} = \frac{f}{F}$$

$$Su = \frac{f.\,To}{F}.$$

From this value the amount of gastric juice may be obtained from the formula $Ma = To - Su$.

The determination of the acidity of the pure secretion may be calculated as follows:

Let a = the acidity of the expressed gastric contents in per cent.
A = the acidity of the pure secretion in per cent.
To = the amount of expressed contents.
Ma = the amount of secretion contained in the expressed contents.

$$\text{Then, } \frac{a}{A} = \frac{Ma}{To} \text{ and } A = \frac{aTo}{Ma}.$$

By a similar formula the enzyme content of the pure secretion can be calculated quantitatively.

Advantages of the Flour-soup Method for the Bacteriologic Examination of the Stomach

The author has shown, in a recent paper (Münch. med. Woch., 1905, No. 27 and 28), that the flour-soup method is excellent for the bacteriologic examination of the stomach-contents. Stained dry preparations of the siphonage are made. He has convinced himself of the usefulness of the method in conditions belonging to the group of gastric catarrhs and those associated with hypo- and hypersecretion. Active bacterial growth is seen. As the soup in its preparation is sterile, it has the advantage over the ordinary test-meal, which contains many bacteria before its introduction into the stomach. It has been usually assumed that the flora of the stomach was confined to sarcinæ, yeast-cells, and the Boas-Opler bacilli of carcinoma and other conditions of stasis. Other groups of micro-organisms do, however, play a great part, although they are not well characterized, and are perhaps not pathogenic. These may, by their chemical and toxic action, produce disturbances of all degrees, and may be of great pathologic importance. They cannot be detected by the ordinary test-meal by reason of its original content in bacteria. The author recommends the flour-soup method for further examinations of the bacteria of the stomach.

The Objections to this Method

Almost immediately upon the publication of the method just described its accuracy was attacked by various authors who had not sufficiently tested it. The chief objection made was that the mixture of the test-meal and gastric juice separated into layers within the stomach, so that a homogeneous mixture of the fats and other contents did not occur, and that consequently the fat in the expressed contents could not be taken as an indicator for the test-meal left in the stomach. This objection was based upon the observation that if the test-meal be expressed in two portions, one corresponding to the upper, and the other to the lower, layer, there will frequently be a difference in the amount of fat contained in the two cases. This observation was founded upon fact. A complete homogeneity of the gastric contents is not usually present after the introduction of the test-meal. At the author's suggestion this question has been carefully studied by Seiler and Ziegler, who published their results in a recent article.[1]

It was shown in these experiments that when the contents of the stomach were removed in two portions and the fat-content of the one designated as 1, the difference between the two was represented in 33 cases by the following: $\frac{1}{15}$, $\frac{1}{17}$, $\frac{1}{24}$, 0, $\frac{1}{21}$, $\frac{3}{25}$, 0, $\frac{1}{10}$, $\frac{3}{14}$, $\frac{1}{3}$, $\frac{1}{8}$, $\frac{8}{25}$, 0, $\frac{5}{8}$, $\frac{4}{15}$, $\frac{1}{15}$, $\frac{2}{19}$, $\frac{1}{13}$, $\frac{1}{8}$, $\frac{5}{24}$, $\frac{1}{13}$, $\frac{1}{5}$, $\frac{7}{26}$, $\frac{1}{21}$, $\frac{8}{13}$, $\frac{1}{6}$, 0, $\frac{2}{25}$, $\frac{1}{12}$, $\frac{3}{16}$, $\frac{7}{25}$, $\frac{7}{34}$.

These investigators used the most unfavorable conditions for their tests. The upper layers were siphoned off, and only small portions of 30 to 50 cc. at a time were removed. Saliva or gastric mucus would, therefore, have a great influence on the results. In spite of this the variations were extremely small, and when it is considered that for clinical purposes the results are only required to be accurate to $\frac{1}{4}$, it will be seen that in most of the cases this difference was not exceeded. In only six cases was the difference greater. The maximum difference in the two siphonages was $\frac{1}{3}$. This may have been due to the admixture of mucus or of saliva. In fact, in both cases the upper layer contained the less fat. In one case the clinical notes mentioned that there was much hypersecretion.

If we designate the relation of the two layers as n, m, we may calculate the influence which the two layers have. Practically, this is not necessary, as in practice the whole contents are removed at the one time. In order to point out the errors of those who have criticized the method it is necessary to take up the mathematics of the question. Taking the difference of the layers Su, Ma, and A, we can calculate these values for f (fat-content) and $\frac{n}{m} \cdot f$. Then one obtains:

[1] Deut. Arch. f. klin. Med., 1904–05.

$$Su_1 = \frac{f.To}{F} \text{ and } Su_2 = \frac{\frac{n}{m} fTo}{F} \therefore Su_2 = \frac{n}{m} Su_1.$$

$$\text{also } Ma_1 = To - Su_1 \text{ and } Ma_2 = To - \frac{n}{m} Su_1.$$

$$A_1 = \frac{aTo}{To - Su_1}. \qquad A_2 = \frac{aTo}{To - \frac{n}{m} Su_1}.$$

One sees that the most important value Su in the maximum error due to stratification is $\frac{1}{3}$ of the fat content. If only a part of the contents of the stomach be removed, the values may vary between 2 and 3. Even as great a variation as this is not of great importance in practice. The errors in the values Ma and A, as the formula shows, are influenced by the errors in the size of To and the error in the estimation of fat. The smaller they are the larger is To.

This calculation of the maximum error, where the relations stand as 2 : 3, place the method in an unusually unfavorable light, but as this variation occurs seldom, and as the total contents of the stomach are removed at one time, it appears that this error may be assumed to be almost infinitely small. It seems that in this regard the critics of the method have totally misconstrued it. It might have appeared that in the now discarded method of estimating the rest of the stomach-contents that the author has suggested partial siphonage, but this was not the case. All the investigations of the stomach-contents which were carried out in the author's clinic were done with the total contents of the stomach. This was very clearly pointed out in the paper of Seiler and Ziegler, who removed the contents in the knee-chest position, withdrawing the stomach-tube gradually. This may be done more easily with a tube containing more than one opening. The rest estimation simply takes into account the small deficit in the siphonage. For the total calculation it is of minor importance. The author wishes to point out again the importance of the procedure which he has recommended for completely emptying the stomach.

If it be objected that although in the perfect siphonage of the stomach the error due to time of removal is eliminated, yet one does not exclude the fact that during digestion the fat and the other materials in the stomach are not perfectly mixed, and thus the whole examination is rendered illusory, it can be shown that this criticism does not hold. The method only gives the conditions in the stomach at the time of the siphonage. The experiments of Seiler and Ziegler showed that the layers which were richer in fat were not always the upper ones. Hence the question of stratification can only be concerned with the idea that particles containing much fat rise to the top, while the rest of the flour falls to the bottom of the stomach, and may at the same time carry fat with it. As a consequence of the irregularity of the findings, both are probably excluded. The differences are probably due to the increased secretion of the gastric juice at certain places, and its incomplete mixture with the flour soup. The final mixture of the contents of the stomach before the estimation of fat brings all these differences to a practical zero. The imperfect homogeneity of the contents is due to regional differences in the secretion of gastric juice. This was shown by Seiler and Ziegler. They made experiments in which the patient changed his position every five minutes. The change in position did not markedly affect the differences in the fat estimations. Seiler and Ziegler have shown what small movements of the stomach are sufficient to prevent sedimentation. They carried the contents of the stomach about for twenty minutes. The movements of walking were quite sufficient to prevent stratification. This would also be done by the slightest peristalsis of the stomach. In decided motor insufficiency of the stomach one might have stratification. In these cases one might not have a true picture of the gastric motility. In spite of this the flour soup method has the advantage over others in that at the end it differentiates stagnation from secretion. Prym has tried to show, with experiments on dogs, using portions of soup colored with different dyes, that the portions recovered still retained their original color. This is a confirmation of the fact that stratification did not occur. Had such taken place, the whole of the contents of the stomach would have been uniform in color. The author does not believe that thorough admixture of the contents of the stomach occurs by peristalsis. Finally, Strauss and Leva have endeavored to replace the present method, using rusks with fat. This seems to be a step backward, as the solid rusks sink in the stomach, and are

incompletely recovered by siphonage. In previous editions the author suggested changing the position of the patient during digestion in order to overcome the effects of gravity. Experiments which have since been made make this procedure absolutely unnecessary.

Normal Results with the Use of this Method as a Foundation for Interpretation of Pathologic Results. Examples for Diagnostic Use and the Value of the Method

The acidity relations of the siphoned gastric contents, using the flour soup, are, as has already been said, the same as when the Ewald-Boas test-meal is employed. The flour soup produces quite as great a gastric stimulus as the bread and tea test-meal. The acidity values are about alike. Some patients may give higher values with the one, some with the other. This is not of importance because the same patient will give somewhat variable results with the same test-meal when it is administered at different times.

As normal results, the following figures found by Seiler in experiments upon normal individuals may be given:

Number.	Amount of soup introduced.	Total stomach-contents, including the residue, after one hour. *To.*	Content of soup in the stomach-contents. *Su.*	Content of gastric juice in the stomach-contents. *Ma.*	Acidity of the pure juice. Per cent. HCl.
1.....	300	124	72	52	0.35
2.....	300	158	83	75	0.44
3.....	300	57	30	27	0.35
Average	.....	113	62	51	0.36
4.....	250	113	44	69	0.32
5.....	250	108	56	52	0.42
Average	....	110	50	60	0.37

If we consider 300 cc. of flour soup as the standard amount ingested, then we can calculate from these and other experiments the average value of *To* after the expression in one hour to be a little more than 100 cc. This volume is divided normally into approximately equal parts of secretion and soup. Nevertheless, it is the common experience with the ordinary test-meal that the amount of the expressed contents varies greatly, even under apparently physiologic conditions, so that only considerable variations from the normal are to be considered pathologic. It is to be noticed that the relation of the amount of secretion to that of soup is far more constant under normal conditions than the amount of *To*. Free hydrochloric acid should, as already mentioned, always be present. The acidity for the normal pure gastric juice varies between 0.32 and 0.44 per cent. These figures stand between those which Pawlow obtained for the normal gastric juice of the dog (0.5 per cent.), and those which Schüle and Troller found in human gastric juice, which they caused to be secreted reflexly by chewing certain substances (0.18 to 0.36 per cent.). That the values of Troller and Schüle are, upon the whole, smaller than the author's is explained by the fact that the mere chewing of substances which cannot be considered as food (lemon-peel, mustard) cause a slighter secretion than an actual meal.

In his last edition the author suggests that a diagnosis of hyper- or hypoacidity should not be made from the hydrochloric-acid content of the total stomach-contents, but that the amount which was present in the pure gastric juice should be calculated. This suggestion has not proved to be practical, for, in the first place, it is against the common usage, and, therefore, leads to confusion, as up to this time the diagnosis of hypo- and hyperacidity have been made from the analysis of the total contents of the stomach. He now suggests that the anomalies in secretion which are made out by means of the flour-soup test-meal should be designated by the words hyper- and hypoacid secretion. By the term hypoacid secretion is understood a deficiency in the acid content of the pure gastric juice. By the terms hypo- and hypersecretion or hypo- and hyperachylia are understood the changes in the volume of gastric juice. As a basis for this estimate we should not take the absolute amount of gastric juice found in the stomach after an hour, but, better, the amount of gastric juice in proportion to that of the soup still present in the stomach. It is this relative amount which is of value for judging the secretory power of the stomach, because, while at every moment a mixture of gastric juice and soup is being removed into the intestine, still the relative amount of soup and gastric juice expressed is not influenced by the motility. Seiler is quite right to call this relation of the volume of secretion to that of the flour soup remaining in the stomach the "secretion quotient." This is normally not far from 1. Considerable variations above 1 would argue for the diagnosis of hypersecretion; below 1, for the diagnosis of hyposecretion.

The motility of the stomach may then be said to be normal if, after the ingestion of 300 cc. of flour soup, not more than 100 to 150 cc. can be expressed at the close of one hour, of which about one-half consists of soup. Therefore, the ratio of the amount of juice to that of soup recovered, as expressed by the secretion quotient, must be considered in the estimation of the motility. For example, if the amount of soup remaining be absolutely normal, but a relatively greater amount of juice be found, this amount of soup points not to a normal, but rather to a hypermotility. So a normal amount of soup with diminished secretion points to a decreased motility. The ratio of the amount of soup removed during one hour from the stomach into the intestine to the amount of soup ingested, $\frac{300 - Su}{300}$, may be called the motility quotient. This varies normally between three-quarters and nine-tenths, and must be interpreted, as has been said, by the consideration of the secretion quotient.

It is evident from the above that it is possible to discover by this method a number of conditions which must have completely escaped the older methods of investigation. By it it is possible to decide whether an increase in the amount of the expressed stomach-contents points to a hypersecretion or to a motor disturbance. It is also possible to discriminate more exactly than before between hypersecretion and hyperacidity, since the volume of secretion, as well as the acidity of the pure gastric juice can be differentiated. Experience with this method has shown us already that gastric disturbances are decidedly more complicated than had heretofore been imagined. The more exact differentiations it enables us to make will, in the future, increase our therapeutic possibilities. It has shown us, for example, that there are

cases of hypersecretion with hypo-acidity, and cases of hyposecretion with hyperacidity.

This condition is possibly due to an abnormal watery osmosis, to which we have previously referred, and which we have traced to an insufficient absorption of the soluble products of digestion. (See p. 488, foot-note.)

These conditions, by the old methods, gave apparently normal results, because in such cases the amount of secretion and the acidity of the gastric juice in mixed gastric contents completely neutralized each other in the determination of the total acidity. To these belong in greater part those cases diagnosed usually as sensory neuroses, in which, in spite of disturbances of digestion, the examination of the stomach-contents by means of the usual methods furnishes completely normal results. That the present simple and insecurely founded classification of the symptomatology of the diseases of the stomach into increased or decreased secretion and excessive or diminished motility must suffer decided alteration may be shown by the following scheme of some functional diagnoses which we are in the position to make by means of the new method:

A. Cases with Sufficient Motility.

1. Hypersecretion with hyperacidity and hypermotility.
2. Hypersecretion with hypo-acidity and normal motility.
3. Normal amount of secretion with hypo-acidity and hypermotility.
4. Hyposecretion, hyperacidity, and normal motility.
5. Hyposecretion, hypo-acidity, and normal or increased motility.

B. Cases with Insufficient Motility.

6. Diminished motility, hypo-acidity, and hyposecretion.
7. Diminished motility, nearly anacidity, and hypersecretion.

More extended experience will certainly tend to give still more combinations.

From the preceding recapitulation it is evident how poorly founded is the attempt of certain authors to ascribe the conditions of hyperacidity and hypersecretion to primary motor disturbances, even narrowing the cause to pyloric stenosis, a view which has often led to gastro-enterostomy in cases where such an operation was not at all justifiable. These more exact functional diagnoses in stomach disturbances are important also in a therapeutic connection. Above all, they indicate clearly whether it is best to influence the motility (laxatives, regular expression of stomach-contents) or to affect the secretion (belladonna preparations, alkalis, by employment of means for stimulating the secretion directly by means of the appetite, according to Pawlow [meat extract, bitters.—Ed.]).

Further Value of the Butyrometric Method of Examination as Applied to the Testing of Amylolysis, Absorption of Carbohydrates, Proteolysis, and Absorption of Proteins by the Stomach.

What has already been said concerning the advantages of the butyrometric method of the examination of the stomach-contents by means of the flour-soup meal has not exhausted the possibilities of this method. It is well suited, for instance, to the quantitative testing of the digestion of starch. In fact, the following method is much more exact than those previously employed, although it

must be confessed that it has not been as yet practically worked out. The expressed stomach-contents, as well as the undigested flour soup which was retained as a control, are examined butyrometrically for their fat-content. Then equal volumes of both of these fluids are measured off, each thrown upon a separate filter, and washed with water so long as the filtrate still shows a starch or sugar reaction. This is to remove the soluble products of the starch digestion. In the residue on the filter in each case the starch content relatively to the content of the insoluble carbohydrate is determined, and the difference in the two amounts calculated for the unit of the fat-content shows how much of the starch has been transformed in the stomach into soluble carbohydrates, *i. e.*, has been digested.

The soup meal can again be employed for the determination of the power of absorption of the gastric mucosa for soluble carbohydrates. Equal amounts of the expressed and retained flour soup are hydrolyzed, and in each the sugar tested quantitatively. The amount of fat in the two fluids must also be determined butyrometrically. The content of sugar which is found in the expressed contents serves as a measure of the total soluble and insoluble carbohydrates which were contained in the stomach and not absorbed. If we therefore subtract this amount, calculated for the unit of fat-content, from the sugar of the undigested flour soup, expressed in the same way, there will be obtained the amount of the absorbed carbohydrate in terms of the unit of fat-content.

In order to understand this value correctly it must be emphasized that the carbohydrates which are introduced by this method into the stomach do not, for the most part, occur in a preformed absorbable form, so that the power of absorption, as found, appears at the same time as a function of the digestion of carbohydrates. If one wishes to determine the amount of the absorption by itself, as by the v. Mering method of determination, it must be considered how much soluble carbohydrate is contained in the ingested flour soup and how much of carbohydrate was transformed into a soluble condition during the digestion.

The interpretation of the relations of carbohydrate digestion and absorption may be shown in the following way:

Let C_1 = the carbohydrate of the undigested flour soup.

Let C_2 = the carbohydrate of the undigested flour soup minus the soluble carbohydrate.

Let C_3 = the carbohydrate of the expressed flour soup.

Let C_4 = the carbohydrate of the expressed flour soup minus the soluble carbohydrate. Then $C_2 - C_4$ = a measure of the carbohydrate that has been digested, *i. e.*, rendered soluble.

And $C_1 - C_3$ = a measure of the absorbed carbohydrate.

$$\frac{C_1 - C_3}{(C_1 - C_2) + (C_2 - C_4)} = \frac{\text{carbohydrate absorbed}}{\text{carbohydrate originally soluble and that dissolved}} =$$

the absorbed fractions of the carbohydrate originally soluble and dissolved during the digestion.

This latter fraction, in an analogous manner to the secretion and motility quotient, may be called the absorption quotient of the carbohydrate.

Finally, the butyrometric determination can be used to test the digestion and absorption of proteins under natural conditions. Here also the method must be more thoroughly worked out technically, but the plan of the examination appears to be clearly outlined. The process is entirely analogous to that for testing the carbohydrate digestion. After the fat in the undigested flour soup, as well as in the expressed stomach-contents, has been determined, each fluid is filtered, and washed free from soluble proteins with water. In all four tests the nitrogen content as determined by the Kjeldahl method serves as a measure of the total proteins, including proteoses and peptones. All of these values must be calculated for the unit of fat-content.

Let N_1 = the nitrogen content of the undigested flour soup.

Let N_2 = the nitrogen content of the undigested flour soup minus the nitrogen of the soluble proteins.

Let N_3 = the nitrogen content of the expressed stomach-contents.

Let N_4 = the nitrogen content of the expressed stomach-contents minus the nitrogen of soluble proteins.

$N_1 - N_2$ = amount of soluble nitrogen in the undigested test-meal.

$N_2 - N_4$ = amount of digested, *i. e.*, soluble, nitrogen.

$N_1 - N_3$ = amount of resorbed nitrogen.

$$\frac{N_1 - N_3}{(N_1 - N_2) + (N_2 - N_4)} = \frac{\text{absorbed } N}{N \text{ soluble and that dissolved}} =$$

the measure of that part of the soluble nitrogen, both that preformed and that made soluble by digestion, which was absorbed. This may be called the *absorption quotient* of the proteins.

Concerning the Technic of the Necessary Determination of Carbohydrate in These Examinations.—This determination can be carried out accurately only if the carbohydrate be completely transformed into glucose and determined as such. For this purpose, according to the method of Pollitz, 20 cc. of the stomach-contents or flour soup are treated with dilute sulphuric acid until the appearance of the positive Congo-red reaction, then further diluted with 40 to 50 cc. of dilute sulphuric acid (5 cc. of dilute sulphuric acid, specific gravity 1160, diluted up to 250 cc. with water), and the mixture heated for eight hours at 108° to 110° C. in a Lintner pressure flask in a paraffin bath, until a color is no longer obtained when iodin is added to a small portion.

Pavy's method is used for the determination of the glucose in the solution. (See p. 620.) Not only albumin, but proteoses and peptones must be removed. After many experiments the author has found that the removal of the proteins, as well as the albumoses and peptones, can be best accomplished by the filtration of the mixture, thorough washing with water, and final treatment of the filtrate and washings with a solution of phosphotungstic acid[1] until no further precipitation occurs. The solution must not contain hydrochloric acid. We cannot, therefore, employ hydrochloric acid either for the hydrolysis or for the acidification of the phosphotungstic acid solution.

After the precipitation of the proteins, the phosphotungstic acid must be removed from the filtrate.[2] This is best accomplished by adding barium carbonate so long as an effervescence takes place. The filtrate from this precipitate should be neutral and free from proteins, and can be employed for the determinations of sugar according to Soxhlet-Allihn, colorimetric or iodometric methods.

Where it is simply a question of the determination of the insoluble starch in the expressed meal in comparison with that in the ingested flour meal, the starch can be approximately determined colorimetrically as iodostarch, according to the usual method of Ambuhl.[3] But since the stomach-contents always contain erythrodextrin in soluble condition, and since this substance, when iodin is added to the expressed meal, causes a dirty brownish-violet color instead of a pure blue, the colorimetric determination of the starch must be undertaken after the soluble starch derivatives, especially the erythrodextrin, have been removed. This can best be accomplished by repeatedly washing the expressed contents with small amounts of water in the centrifuge. It must be mentioned that the exact separation of the solid from the soluble constituents by means of the centrifuge is successful only when the expressed contents have been extracted with five volumes of ether for the separation of the fat (by means of the separatory funnel, p. 451). One cubic centimeter of the undigested and of the expressed flour soup are exactly measured off by means of a pipet calibrated to hundredths of cubic centimeters, washed with water, and then with ether until a test of the substance remaining shows a pure blue color. The remaining part is boiled for ten minutes with about 500 cc. of water, during which the greater part of the starch passes into solution. After cooling, diluted Lugol's solution is added drop by drop to both tests until the blue color does not become more intense. The shades of color of the two fluids are then compared colorimetrically, and it is determined in a measuring cylinder how much the darker fluid must be diluted in order to correspond exactly to the shade of the other. The rates of dilution necessary for this purpose gives directly the ratio of the amount of starch in the ingested to that in the expressed meal.

Special Examination of the Stomach for "Gross Motility"

Those cases in which the ability of the stomach to empty itself is impaired, and where pyloric stenosis is not present, are frequently spoken of as insufficiency or motor weakness of the stomach. We have learned from von Mering,[4] Hirsch,[5] and Marbaix[6] that the emptying of the stomach is regulated by the intestine rather

[1] One part of phosphotungstic acid diluted with 20 parts of water and acidified with sulphuric acid.

[2] It is only in the determination by means of the polariscope, which for this purpose is hardly accurate enough, that the phosphotungstic acid need not be separated, since it has no effect on the plane of polarized light.

[3] Cf. Schweiz, Lebensmittelbuch, Bern, Verlag v. Neukomm und Zimmermann, 1899.

[4] Cong. inn. Med., 1893, 470.

[5] Cent. f. inn. Med., 1892 and 1893.

[6] La Cellule, 1890.

than by the stomach itself, since nutritive substances reaching the intestine effect a reflex closure of the pylorus (von Mering's reflex) until the intestine has completed its work. It consequently seems to the author to be inadmissible to regard the emptying of the stomach as a pure question of strength, as would be suggested by the term insufficiency or motor weakness of the stomach, since even a well-developed and efficient stomach does not empty itself if it be opposed by the intestine. Actual weakness of the stomach nevertheless does occur, and, in order to differentiate it from the more frequent forms of disturbed motility which proceed from the intestine, a special method of examination is necessary, which the author will now give, and which he has carefully tested in recent years. The motor activity of the stomach must be examined under conditions in which von Mering's reflex does not occur. As von Mering and Marbaix have shown, such a condition is present when the stomach contains water alone, since, under physiologic conditions without obstruction, the water is emptied into the intestine within a short time. We must consequently determine the length of time required by the stomach to empty itself of a definite quantity of water—a half liter, for example.

Since we have to do with stomachs which do not empty themselves well, the test must be preceded by a thorough cleansing of the organ. The stomach must be completely emptied of the rinsing water by the method described on p. 445. The patient then drinks the prescribed quantity of water, the gastric contents are then expressed in a half-hour, and the quantity passed onward into the intestine is thus determined. Here also the above-mentioned method is used to evacuate the stomach. The residue estimation, using methylene-blue, which was suggested in previous editions of this book, is quite unnecessary. The method has therefore gained in simplicity.

The test for "gross motility," must be carried out with the patient in the upright position, since gravity interferes too much with the expression if the patient be lying down.

Special Examination of the Stomach for Pyloric Stenosis

Pyloric stenosis is diagnosed much too frequently nowadays when the stomach fails to empty itself properly. In reality the case may be simply a functional disturbance of von Mering's reflex or a condition of motor weakness. It is, therefore, desirable to be able to detect stenosis directly. Moritz has shown that the stomach is an excellent sedimenting apparatus, and that in all forms of impaired motility firm, indigestible substances (fruit kernels and other vegetable constituents) may remain in it for days, since they are never elevated to the level of the pylorus on account of their high specific gravity. We are consequently not justified in diagnosing a pyloric stenosis offhand from the presence of such old substances in the retained gastric contents. A little reflection will also show that the retention of indigestible substances of a specific gravity low enough to enable them to float may be utilized to diagnose a pyloric stenosis the caliber of which is not sufficient to allow of their passage. This is the basis of the procedure the author recommends, by which it is possible to diagnose the existence and caliber of a pyloric stenosis by the administration of little balls of cork. The patient to be examined for pyloric stenosis is made to swallow a ball of cork 1 cm. in diameter. If the cork ball be found in the stool the following day, the pylorus must be large enough to have allowed it to pass. On account of its low specific gravity, the cork ball may easily be found, since it readily floats when water is added to the stool. If, however, the ball be not found in the stools after several days and the administration of a spoonful of castor oil, a stenosis of the pylorus of less than 1 cm. is indicated; for even in the most severe disturbances of gastric motility if the latter be not associated with stenosis the sphere, on account of its low specific gravity, does not sink to the low-lying portions of the stomach and remain there, but finds its way into the intestine. Certain precautions must be observed, however, in carrying out this test. After swallowing the cork the patient should lie in bed for a half-day, preferably upon the left side, so that the ball may be floated upward into the neighborhood of the pylorus. If the stomach is markedly loop-like, it may be sufficient to have the patient lie upon the left side for a short time, under the supposition that the cork ball is immediately floated toward the pylorus and remains there. The author has not yet employed cork balls larger than 1 cm. in diameter, for fear they might stick in the esophagus. To what extent the caliber of the ball may be increased remains a subject for further study.

Recently, the author has modified the method by using, instead of solid pieces of cork, sacs of rubber containing cork filings made like the desmoid sac, which are

tied with a piece of catgut the size of a D violin string which has been hardened in 2 per cent. formol solution for two hours. This method is suggested in order to avoid the permanent remaining of a solid piece of cork in a stomach with a pyloric stenosis. This might float to the pylorus, and acting as a valve, increase the occlusion. Catgut hardened in formaldehyd is very difficultly digestible in the stomach and also in the intestine. It is, however, finally dissolved, and can thus produce no harm. In order to ascertain whether the retention of the sac has been due to failure of solution of the catgut or to occlusion, a methylene-blue pill is given not weighted with bismuth. This is included in the sac. One then finds out whether the catgut has been dissolved, from the appearance of the pigment in the urine. The sac must be prepared with especial care in order to prevent the inclusion of particles of cork in the neck. This can be avoided by wrapping them first in a layer of tissue-paper. This process has often been of great diagnostic value, where it was wished to distinguish between functional disturbance in the emptying of the stomach and a pyloric stenosis.

DETECTION OF CERTAIN POISONS IN THE GASTRIC CONTENTS OR THE VOMIT

ARSENIC

In most cases of acute arsenic poisoning, arsenous acid has been used. This may often be found as white, insoluble particles which can be identified chemically. If the arsenous acid has been used in solution, the metal may be detected by boiling the suspected material with a piece of copper foil. The foil will be covered with a gray layer of the amalgam of arsenic with copper. Solid particles are introduced into a piece of hard glass tubing drawn out to a point, a small bit of charcoal placed on top, and both are heated gradually in a free flame. In this way the arsenous acid is reduced to metallic arsenic, and a black mirror is produced which is deposited on the glass. The Marsh test is more delicate. A hydrogen apparatus is constructed with a thistle tube and a flask. The outlet tube is provided with a calcium chlorid tube and a piece of hard glass drawn out in the middle. Zinc, free from arsenic and antimony, is placed in the flask, and hydrogen generated with pure dilute sulphuric acid. The hard glass tube is then heated for some time to assure the absence of arsenic and antimony in the reagents used. The material to be examined is then added through the thistle tube. If the substance contain arsenic, arsin is formed. This is characterized by the fact that the flame formed by lighting the gas leaving the tube burns with a bluish flame. If a porcelain plate be held in the flame, a blackish spot due to metallic arsenic is formed. A similar spot is formed by antimony. The latter is distinguished by the fact that it is only slowly soluble in sodium hypochlorite. If the tube itself be heated, an arsenic mirror is formed beyond the point of heating.

HYDROCYANIC ACID AND POTASSIUM CYANID

Hydrocyanic acid and potassium cyanid after the acidification of the contents of the stomach are characterized by the smell of bitter almonds. To detect these substances, the acidified mixture is distilled, and the distillate made alkaline with sodium hydroxid. Ferrous sulphate solution is then added. The mixture is then made acid with hydrochloric acid, and a drop of ferric chlorid added. In the presence of hydrocyanic acid Prussian blue is formed. The acid may also be detected by adding to the distillate a few drops of ammonium sulphid. The solution is then evaporated to dryness, a small amount of hydrochloric acid added, and a drop of ferric chlorid. In the presence of hydrocyanic acid, a blood-red spot due to ferric thiocyanate is produced.

ATROPIN AND HYOSCYAMIN

The contents of the stomach are first rendered alkaline and extracted with chloroform or benzin. By evaporating the chloroform solution, a residue is left which will produce mydriasis when introduced into the eye of a cat.

CHLORAL HYDRATE

The contents of the stomach are rendered alkaline with sodium hydroxid, and distilled at 60° to 65°. Chloroform is formed, which is recognized by the smell and by the following reaction: To the distillate add a little anilin and alcoholic potassium hydroxid. The intense penetrating odor of phenyl isocyanid is produced.

The chloroform vapor may be led through a heated tube into a solution of starch and potassium iodid. The free chlorin formed by heating the chloroform liberates free iodin, which produces blue iodid of starch. Chloral hydrate may be extracted from the gastric contents by ether. In this method, which involves the conversion of chloral hydrate into chloroform, preformed chloroform must be excluded by the odor and by the reaction performed before distillation. Chloral hydrate may be extracted from the gastric contents with ether, and may subsequently be detected in the ethereal residue after evaporation by dissolving the residue in water and adding ammonium sulphid. A brown precipitate is formed, and an unpleasant and characteristic odor is developed.

POTASSIUM CHLORATE

The solution to be examined is made distinctly acid with sulphuric acid, and indigo dissolved in fuming sulphuric acid added, and finally, a solution of sodium sulphite. The color of the solution is changed to green or yellow. The potassium chlorate may be separated from the mixture by dialysis, and the substance detected in the dialysate.

OPIUM

The presence of opium may be suspected from the characteristic odor and the yellow color in the case of laudanum administration. The detection of opium and morphin by exact methods will be found in Witthaus and Becker, System of Legal Medicine and Toxicology.

PHOSPHORUS

The investigation should take place with as fresh materials as possible. The solutions containing it are often phosphorescent in the dark. The substance may be detected by the following methods:

Scherer's Method.—The contents of the stomach are shaken with a little lead acetate solution, to remove hydrogen sulphid, and the mouth of the flask closed with a piece of paper moistened with silver nitrate solution. The whole is allowed to remain in the dark for some time. With traces of phosphorus, the paper is stained black.

Mitscherlich's Method.—The contents of the stomach are made acid and distilled in the dark. The condenser will contain a luminous ring. Small amounts of alcohol, ether, and oil of turpentine, which may be present in the contents of the stomach, will prevent the reaction.

Dusart-Blondlot's Method.—This method is based on the fact that small quantities of phosphorus render a colorless hydrogen flame distinctly green.

MERCURY

The detection may be made with brass gauze, but it is necessary first to destroy the organic substances in the mixture. This is done by the method of Fresenius and von Babo. To the contents of the stomach are added $\frac{1}{3}$ to $\frac{1}{2}$ the volume of concentrated HCl and 20 gm. of potassium chlorate. The mixture is heated in a porcelain dish on the water-bath, and at intervals of from five to ten minutes 0.5 to 2.0 gm. of potassium chlorate are added, until the liquid is clear and of a straw yellow color. Water must also be added from time to time. Two gm. of chlorate are again added, the fluid allowed to cool, and strained through a cloth. The mixture is heated on the water-bath until the smell of chlorin has disappeared. The liquid can now be tested for mercury with brass gauze. In most cases of poisoning with mercury the substance used is sublimate. This is soluble in ether, and may be directly extracted from the fluid with ether. On evaporating the ether the crystals of sublimate remain. This may be identified by the red precipitate given by potassium iodid, which is soluble in excess of the reagent.

STRYCHNIN

The solution is made alkaline with ammonia, and extracted with benzol. The physiologic test can be applied to the residue. Frogs injected with the solution are attacked with tetanic convulsions. Only 0.005 mg. of strychnin are necessary to produce the result. Chemically, the substance may be detected by extraction with ether. To the residue a drop of sulphuric acid is applied, and a minute crystal of potassium bichromate added. In case strychnin be present, a violet color is produced.

EXAMINATION OF THE INTESTINE AND FECES

Inspection, palpation, auscultation, and percussion of the abdomen and their help in the examination of the intestine have already been considered upon pp. 368 et seq., 371 et seq., 352 et seq., 257 et seq., and 277 et seq.

Hence, we will now discuss only the local examination of the rectum (digital and speculum examination), the testing of the intestinal functions, and the examination of the feces.

LOCAL EXAMINATION OF THE RECTUM

DIGITAL EXAMINATION OF THE RECTUM

The examiner ordinarily employs the index-finger, well lubricated, and, of course, with a carefully cut nail. The finger may be protected by employing the ordinary thin rubber finger-cot. Surgeons and obstetricians do well to employ a thin rubber glove, thus protecting the proximal end of the finger as well. The patient may be in the dorsal decubitus with the legs widely separated, resting upon the small of the back (the latter is advisable, so that the examiner's elbow shall not prevent his palpating the anterior rectal wall). If, as is sometimes more convenient, we examine with the patient in the lateral position, the knees should be well drawn up to allow room for the examiner's arm in all directions. The knee-chest position, which has recently been so frequently employed by the gynecologists, is also to be recommended, since it displaces the intestinal coils upward and facilitates the palpation of the pelvic viscera. For different purposes and under different conditions these positions can be varied and the examiner's hand changed; the important thing is that the entire circumference of the rectum must be palpated, and we must be able to reach up with the finger as far as possible. The anal opening should be inspected before performing the digital examination, as we can thus often recognize the presence of hemorrhoids, prolapsus, fistula in ano, or fissures.

Separating the folds of the buttocks with one hand, the finger should be introduced slowly and carefully with a gentle, screw-like motion, so as not to cause pain or injury. Beginners often make the mistake of not following the axis of the rectum after introducing the finger, especially when they try to palpate as high up as possible. They will then fail to reach up very far, and so may even believe that they have found a stenosis, though none is present. The anatomic position of the rectum should be remembered, and this error will be prevented. The direction is first a little forward from the anal opening, then backward into the hollow of the sacrum, and finally to the left toward the sigmoid flexure. While advancing the finger we must remember to keep it always in the middle of the funnel formed by the mucous membrane. If feces be present, they will be the best guide as to the direction in which to advance the finger. The height to which the palpating finger may reach depends upon various factors: an examiner's thick, short fingers and the patient's excessive fat are the chief obstacles. Sometimes the pain of the procedure or the spasmodic

contraction of the external sphincter will prevent an effective examination. Only in exceptional cases is it allowable to introduce two fingers. The introduction of the whole hand under anesthesia (after Simon) has, so far as we know, been discarded as too dangerous a method.

Digital examination reveals, first of all, the more crude anatomic changes—carcinoma of the rectum, other tumors and ulcerations of the rectum, rectal polyps, which are not situated too high up, an invagination which has reached down as far as the rectum. Large internal hemorrhoidal masses may also be felt; but unless thrombosed, it requires considerable experience to differentiate them with certainty from the normal inequalities and folds of the rectal mucous membrane. Superficial ulcerations are quite as difficult to appreciate by palpation.

In a case of intestinal obstruction, *considerable distention of the rectum* points strongly to fecal rather than some other type of intestinal obstruction. If fecal masses have pushed down into the rectum and the general symptoms of obstruction have improved, our prognosis immediately becomes more favorable, even before any feces have been evacuated. An extremely painful digital examination would suggest inflammatory changes of the rectum. If slimy, purulent, or bloody masses adhere to the finger when withdrawn, this diagnosis is still more strongly suggested. A microscopic examination of the material adhering to the withdrawn finger will sometimes aid in the diagnosis of tuberculous or dysenteric changes, and perhaps be more serviceable than the examination of the feces, especially if the rectum has been just cleaned of fecal matter by an enema (pus, tubercle bacilli, amebæ, oxyuris). (Compare Examination of Feces, p. 510.)

A careful rectal examination is important in diseases of the nervous system. The degree of impaction in the rectum, the sphincter tonus, and the sensitiveness of the rectal mucous membrane tell of the condition of the rectal activity (function). This information is the more important as the character of defecation and the shape of the stools depend not only upon the rectal innervation, but upon the influence of the bowel above.

In examining the rectum we must also try to obtain information regarding the condition of the adjacent organs: the prostate and seminal vesicles in the male, the uterus, tubes, and ovaries in the female. In a virgin, as a rule, a pelvic examination by palpation can be successfully accomplished only by way of the rectum.

EXAMINATION WITH THE SPECULUM AND WITH THE PROCTOSCOPE

With the aid of a so-called rectal speculum the examiner can see the inner surface of the rectum directly. Rectal specula are made quite like vaginal specula—tubular, bivalve, duck-bill-shaped, or many valved. They may also consist of two separate spoons. The speculum should first be warmed and well oiled, and then carefully introduced into the axis of the rectum. With an ordinary head-mirror a good light can be reflected, and the rectal mucous membrane at the end of the speculum carefully examined. The position of the patient will be varied according to the part of the rectum to be examined, either the lateral, the usual dorsal gynecologic position, or sometimes the knee-chest position. The advantage of the knee-chest position is that the rectum is relieved by the intestines dropping forward, and so is more accessible to examination. In difficult cases the speculum examination should always be tried in this position and with the pelvis elevated. The speculum should be introduced very carefully and slowly. The many-valved specula must be furnished with an obturator before being introduced, and also before each further advance, for otherwise they are apt to pinch and injure the mucous membrane.

Examination with a speculum is difficult on account of the limitation of the field of vision, and the fact that the parts are usually in an abnormal position and under abnormal tension, so that the interpretation of the findings is difficult. Peristalsis of the rectum is often caused by the irritation of the speculum, especially in inflammatory affections, so that it is very difficult to adjust the instrument. Palpation reveals many of the changes, but others most essential to determine, such as inflammatory congestion and superficial ulcers which are not palpable, are often very difficult to recognize with this instrument, for its pressure causes considerable congestion, altering the color, and in the case of ulcers oftentimes brings on hemorrhage, which covers the field of vision again and again even if sponged off continuously. In these conditions severe pain usually interferes with the speculum examination. The tubular and the many-valved specula frequently furnish incorrect conclusions because the mucous membrane prolapses within the instrument in irregular folds. The bivalve, duck-billed specula, by means of which a part of the mucous membrane smoothly stretched can be exposed to view, are rather better. The examination is most conveniently made in the knee-chest position, with the instrument consisting of two separate spoons, but its employment always requires the aid of an assistant.

The results of the ocular inspection of the rectum have been essentially improved since we have employed modern proctoscopy (see below).

MODERN PROCTOSCOPY, EMPLOYING ELECTRIC ILLUMINATION AND A DEVICE FOR INFLATION[1]

Inspection of the rectum plays an important part in diagnosis since we have substituted for the ordinary rectal specula, whose limitations have been discussed above, the much more reliable rectoscopic instruments perfected by the efforts of Otis, Kelly, Pennington, Laws, Tuttle, and H. Strauss, and since Schreiber's[2] fundamental studies have placed the methods of rectoscopy upon an exact scientific basis in accord with anatomic, physiologic, and clinical obsevations. H. Strauss's so-called proctosigmoidoscope[3] is the most complete and valuable rectoscope. (See Fig. 212 and the following pages.) It consists of a straight metal tube, 35 cm. long and 2 cm. in diameter. It is constructed on the principle of an endoscope, and has an electric lighting attachment. The great length of the tube is an important feature, for it can be introduced into the rectum like a speculum, affording, under favorable conditions, a view 30 or more cm. above the anus. This great length is made practicable by the connection of the interior of the tube with a rubber bag to inflate the rectum with air during the introduction of the instrument and after it is in place. A glass plate closes the outer end of the tube when in use, making the inflation feasible. By this means introduction of the instrument, in spite of the varied curves of the bowel, is facilitated, since further advance can be guided by the eye of the examiner and the tip of the instrument pushed in the direction of the lumen of the bowel as the latter becomes visible through the glass plate. The outside of the tube is marked in centimeters so that the depth of insertion is always evident. Fig. 211 *a* represents the proctoscope tube with its handle and the attached bag, *b*, the metallic obturator which closes the inner end before introduction, *c*, a staff ending in a tiny electric light which is fixed in the interior of the tube, after withdrawal of the obturator by means of a fastening shown in the figure. The light thus rests at the edge of the inner opening of the tube. The dotted lines show the position of the lighting apparatus in the tube. The fastening of the latter supports the glass plate mentioned above, with a bayonet joint. This so-called window, shown at the top of *c*, permits visual examination while the rectum is being inflated. The instrument should be introduced so that the lamp is uppermost. This position renders it less likely to be smeared with feces, which, if present, are more apt to lie in the lower part of the tube. For operative purposes and for cleaning the parts situated within the field of vision it is, of course, necessary to remove the window, and this may be very easily accomplished by loosening the bayonet joint. The instrument can be taken apart for cleaning and the tube itself can be boiled. A pair of specially designed forceps for freeing the visual field are furnished with the instrument. The directions for use are as follows:

[1] References: J. Schreiber, Die Recto-romanoscopie, Berlin, Hirschwald, 1903; H. Strauss, Zur Methodik der Rectoscopie, Berl. klin. Woch., 1903; Tuttle, A Treatise on Diseases of the Anus, Rectum, and Pelvic Colon; H. Strauss, Erfahrungen über die Endoscopie der Flexura Sigmoidea, Berl. klin. Woch., 1905, No. 36.

[2] Die Recto-romanoscopie, Berlin, Hirschwald, 1903.

[3] Made by L. and H. Lowenstein, Zieglerstrasse 28, Berlin.

1. The evening before examination the patient receives an enema of 1 liter, and about three hours before, another of ¼ liter, of physiologic salt solution. Care should be taken that the enema is completely returned. If diarrhea exist, 10 to 15 drops of tincture of opium are given one hour before the operation.

2. The patient is always placed in the knee-chest position, with his head in contact with the table and his legs spread somewhat apart.

3. The instrument with the obturator in position, is first warmed and then lubricated. The patient's anus should also be smeared with vaselin. It is rarely necessary to use cocain, eucain, or anesthesin ointment.

4. The introduction of the instrument as far as the sigmoid is carried out in three steps.

(*a*) Through the perineal portion of the rectum (about 5 cm.), the tube with the obturator in position is held approximately horizontal.

(*b*) Through the ampulla of the rectum (about 6 cm.), the obturator removed and the lamp in place, the tube is guided by the eye. The part of the tube within the rectum is tilted upward.

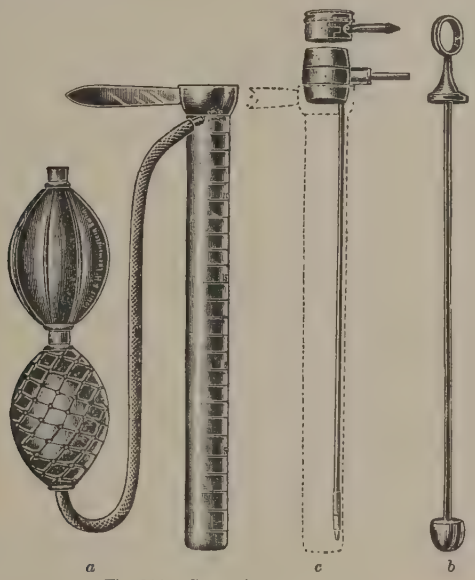


Fig. 211 —Strauss's rectoscope.

(*c*) Through the introitus flexuræ. The assistant now holds the instrument at the mark 11, while the examiner, guided by his eye, brings the tube into a horizontal and approximately median position. A slight lateral movement or one from above downward should now disclose the entrance into the flexure; but if not, the window is inserted and the assistant inflates the bowel with one or two bulbfuls of air while the examiner watches for some movement of the bowel-wall to disclose the entrance and listens for bubbling murmurs.

5. The instrument may now be very gently pushed further into the flexure, under the guidance of the eye, by carefully lifting the outer end, and, if necessary, by further inflation.

6. Fluid or solid feces which obstruct the field of vision may either be pushed aside or wiped away.

7. The character of the mucous membrane is to be noted during the introduction and withdrawal of the instrument.

The knee-chest position recommended by Strauss, though convenient for the examiner, is naturally unsuitable for many patients. In such cases the author has found it convenient to employ the lateral or gynecologic posture. If the latter be selected, the patient's pelvis must project well beyond the edge of the table, to permit

depressing the outside end of the tube during its introduction. The examiner must, of course, work in an uncomfortable position, preferably upon his knees.

Since the introduction of Strauss's rectoscope in the Bern clinic, the author has noted a distinct advance in the accuracy of rectal diagnosis. Instead of the limited view obtained with ordinary rectal specula, where orientation is very difficult on account of prolapsed folds of mucous membrane, one often obtains a clear, free view into a stretched open cavity on the walls of which, with alternate advances and withdrawals of the instrument, not the slightest changes can escape observation. Its chief advantage is, however, that it enables one to examine directly 20 and in many cases 30 cm. of the lower bowel, and to see the lower portion of the sigmoid flexure, while digital examination cannot extend further than 9 to 10 cm. above the anus, and the ordinary rectal specula little further. The use of this instrument materially improves the prognosis of rectal carcinoma because the early diagnosis of high-placed growths becomes possible. Every practitioner should possess one of these instruments, because it is easy to handle and requires but little practice. If electric illumination be not at hand, a head-mirror answers the purpose.

Besides aiding in the diagnosis of rectal carcinoma, the author finds the instrument very useful in recognizing other conditions, *e. g.*, deep hemorrhoids which are not accessible to palpation and which may cause obscure intestinal hemorrhage and anemia; the existence of an intensely red and easily abraded mucous membrane responsible for obscure bleeding; benign growths which, to digital examination, give the impression of malignancy (Schreiber); and Schreiber's interesting findings in oxyuris infection. This writer has determined that it is not possible to introduce rectal tubes above the angle of the sigmoid, and that they are generally obstructed at the junction of the upper and lower limbs. This also holds good for sounding the rectum, even if Kuhn's spiral sounds be employed. (See p. 505.)

The reader who wishes to employ the rectoscope is urged to study Schreiber's fundamental work on rectoromanoscopy (Berlin, Hirschwald, 1903). It contains important statements upon the anatomy and physiology of the rectum, and also a series of interesting rectoscopic pictures which are a good introduction to the method. The author quotes the following anatomic details: The true rectum reaches 11 cm. above the anus; from there the descending limb of the flexure (the part accessible to rectoscopy) stretches to 32 cm. above the anus. The rectum itself is subdivided into the perineal or sphincteric portion and the pelvic portion. The external and internal sphincters, with the so-called intermediate portion, make up the former. The external sphincter is characterized rectoscopically by radial fibers; the internal, by longitudinal fibers. The perineal portion is about 4.5 cm. long, the external sphincter 2 cm., the internal 2.5 cm. Above the latter lies the so-called ampulla of the rectum, in which two constant folds are found, the lower plica coccygea, the upper plica sacralis (inferior). The plica sacralis superior is inconstant. These folds are sometimes to the right, sometimes to the left, but usually on the anterior wall. The ampulla is divided from the sigmoid by the plica rectoromano, lying to the right. The plicæ sigmoidea situated in this limb of the flexure are generally narrow; they vary in number and usually extend over only a quadrant of the tube. A fold of mucous membrane which forms the boundary between the two limbs of the sigmoid generally prevents the advance of the rectoscope more than 32 cm. from the anus.

INSUFFLATION OF THE RECTUM

Inflation of the rectum is best accomplished, as described on p. 373, with a Davidson syringe.[1] It aids in determining the position of the sigmoid flexure and of the colon. When inflated, they can be seen to stand out against the anterior abdominal wall, separate from the surrounding parts, and may be mapped out by percussion and palpation. The position of abdominal tumors, especially in relation to their origin in the colon, the sigmoid flexure, or the kidney (see p. 376), can often be determined by the aid of this method. It does not tell very much about the condition of the rectum itself, even for the diagnosis of stenosis of the rectum. For moderate stenoses—which are just the ones so difficult to diagnose—offer no obstruction to inflation, while very pronounced or impermeable stenoses can be easily enough diagnosed without it. This method is of little value even for determining the seat of such obstruction. If it be impossible to introduce any considerable quantity of air into the rectum, it is generally assumed that the obstruction is situated low down. This, however, is very deceptive, because, if the stenosis be pronounced, there will be so much abdominal distention that it will prevent the distention of the rectum even if the obstruction be high up.

[1] The rectoscope described above answers this purpose very nicely.

INJECTIONS OF WATER INTO THE RECTUM AND RECTAL LAVAGE

Introducing fluids to determine the capacity of the rectum or the seat of a stenosis is even less valuable than inflation, because the rectum is intolerant of fluids in many people and the individual variation is considerable. By irrigating the rectum and then selecting suspicious fragments from the wash-water to be examined macroscopically and microscopically, we can sometimes diagnose a high-seated carcinoma. It is best to cleanse the rectum thoroughly with the help of a mild laxative and an enema a few hours before the examination.

SOUNDING OF THE RECTUM

If an obstruction be situated low down, a rectal bougie will give no more satisfactory results than an ordinary digital examination. If seated higher up, we can never tell accurately whether the bougie is impeded by a pathologic stenosis or by some physiologic obstruction, as is very often the case. The elastic metal intestinal tubes constructed with a spiral spring have been advocated by F. Kuhn[1] for rectal work. Their practical value must be determined after experience in their use. According to J. Schreiber's proctoscopic control (see p. 504), their value is doubtful because it is not certain that they overcome the curving of the sigmoid as the inventor expected. Modern proctoscopy should make sounding the rectum almost unnecessary.

EXAMINATION OF THE INTESTINAL FUNCTIONS

EXAMINATION OF THE MOTILITY OF THE INTESTINES

Inspection and auscultation of the abdomen will tell something about the motility of the intestines. (See p. 368 et seq. and p. 352.) The manner of defecation and the examination of the feces will also aid. (See p. 510 et seq.) Of course, conclusions in regard to the intestinal motility are given by the passage of flatus as well as by the passage of feces. The intestinal motility is certainly not directly proportional to the frequency of passing flatus, for this depends to a far greater degree upon the production of gas in the intestine; yet, at the same time, a free and abundant passage of gas indicates good intestinal motility, while a complete inability to evacuate any flatus, which is so annoying to the patient on account of the associated distention, suggests some impairment in intestinal motility. This latter condition (see p. 511) is important in the types of ileus where solid or fluid evacuations still take place (fecal matter coming from below the obstruction), but where the absence of evacuated gas presents such a contrast as to furnish a very significant symptom of obstruction.

To time the intestinal motility, certain substances, such as charcoal, milk, or lycopodium, are ingested at a definite time, and the stools watched to determine the interval required for these substances to appear. Charcoal will be recognized by the black color, milk by the light-yellow color, and lycopodium by the characteristic tetrad shapes of its spores under the microscope. The charcoal and the lycopodium should be administered (in doses of one-half to a whole teaspoonful in water or in cachets) directly after eating, but the milk in large amounts, between meals, as far apart as possible. Of course, the character of the gastric motility must be taken into account in judging of the results of this test.

EXAMINATION OF THE CHEMISTRY OF THE INTESTINE AND OF ABSORPTION IN THE INTESTINE

The careful examination of the feces will aid in determining the intestinal chemistry, especially with reference to the utilization of the

[1] See Berlin. klin. Woch., 1898, No. 2, p. 27.

food (see p. 505); but the disadvantage of this is that ordinarily we do not consider the influence of the length of time the food constituents remain in the intestine (see above, use of charcoal, milk, etc.). (See p. 542 for the demonstration of the digestive ferments in the stools.) The clinical examination of the chemical changes induced by intestinal bacteria is as yet impracticable (excepting the so-called fermentation test of the feces, see p. 532). Even a tedious complete metabolic determination of the utilization of the nutriments (see the fundamental examinations of v. Noorden[1]) furnishes results both of stomach and intestinal digestion, not of the latter alone; and besides the chemistry, absorption and motility of the digestive tract are also concerned. Neither are we justified in deducing from the amount of urea eliminated the absolute degree of metabolism, nor the sum total of the digestive processes taking place in the organism. (See p. 628.)

EXAMINATION OF THE INTESTINAL DIGESTION BY MEANS OF THE GLUTOID CAPSULES

For a long time the writer has been interested in the problem of obtaining some *direct* evidence in regard to the chemical activity of the intestines, especially with reference to proteid digestion. For the small intestine he has employed the glutoid capsules, which are made from gelatin (glutoid) hardened with formaldehyd. They either do not dissolve in the gastric juice at all, or only after a considerable time, but they are rather quickly soluble in pancreatic digestion mixtures.[2] They take the place of Unna's keratin-coated pills, which have not proved successful. These glutoid capsules may be utilized to diagnose the condition of the intestinal digestion, *i. e.*, the pancreatic function. They are filled with some substance which will not diffuse through the capsule-wall, and whose absorption may be studied from an examination of the saliva or the urine. Substances containing iodin are best adapted for this purpose. Iodoform has given the author the best results. It is absorbed both from the stomach and the intestines in a very short time—within from one-quarter to one and one-quarter hours. After the ingestion of 0.15 gm. of iodoform a marked iodin reaction can be obtained in the saliva or in the urine (especially well in the former) with chloroform, sodium nitrite, and sulphuric acid. (See p. 434.) Iodoform has another great advantage in that it cannot penetrate the glutoid capsules.

Salol answers very well for the same purpose, for, within one to one and one-half hours after the ingestion of 0.5 gm. of salol salicylic acid can be demonstrated in the urine with ferric chlorid as salicyluric acid. (See p. 432.) So that normally after the glutoid capsule has been dissolved by the pancreatic juice the iodin reaction will be demonstrable in the saliva, and the urine, at the latest, within one and one-quarter hours if 0.15 gm. of iodoform has been administered in one glutoid capsule, and the salicyluric reaction can be demonstrated in the urine within one and one-half hours after the administration of 0.5 gm. of salol in two capsules.[3]

In order to make the conditions as constant as possible in regard to the length of time that the capsules remain in the stomach and in regard to the degree of digestive stimulation it is advisable to administer them with an Ewald test-breakfast (p. 444). The author's experience shows that, normally, *i. e.*, under the best

[1] Grundriss einer Methodik des Stoffwechsels, Berlin, 1892; Lehrbuch der Path. des Stoffwechsels, Berlin, 1893; Zeit. f. klin. Med., 1890, p. 137.

[2] Deut. med. Woch., 1897, No. 1; Correspondenzbl. f. Schweizer Aerzte, 1898, No. 10; Deut. Arch. f. klin. Med., 1898, vol. lxi.

[3] Filled glutoid capsules of varying degrees of hardness may be obtained from A. G. Haussmann, in St. Gall, Switzerland. They are tested in the human stomach and their constancy is guaranteed. For diagnostic purposes a capsule of the maximum hardness is requisite. For therapeutic use a much softer one is employed. The purpose for which they are to be used should be stated when they are ordered. The diagnostic capsules which are used most frequently contain 0.15 gm. of iodoform. For use in children capsules are prepared with 0.05 gm. iodoform, and for the urine test capsules with 0.05 gm. iodoform and 0.25 gm. salol. To adults two or three of the latter must be administered at one time in order to furnish a sufficient dose of salol. The following statements in regard to time refer to the hard capsules used for diagnosis.

conditions possible, normal gastric motility, normal intestinal digestion, and normal intestinal absorption, the iodin reaction may be expected to appear in the saliva and the urine, and the salicyluric reaction in the urine, in from four to six hours. To test the reliability of the capsules obtained from the manufacturer it is necessary to prove that the reactions are obtained in this length of time in healthy individuals.

Three hours after the administration and at regular intervals thereafter the patient expectorates saliva or, better, voids urine[1] in numbered beakers. These specimens are examined later for the presence of iodin or salicyluric acid, according to the tests mentioned on pp. 434, 610, and 611. The author has found that iodin elimination by the saliva is so irregular in many individuals that he recommends employing the urine test in preference unless the patient cannot retain his urine or the latter is deeply colored by bile-pigment. The time of voiding the specimen which first exhibits the positive test shows the rapidity with which the glutoid capsule is dissolved, *i. e.*, the intensity of the pancreatic digestion (see certain restrictions mentioned later). Only rough, approximate differences in the time of the reaction are of diagnostic importance, so that it is really sufficient to examine the saliva or urine after six, eight, ten, and twenty-four hours. To make the test as uniform as possible it is perhaps advisable to administer the capsules in the morning with the test-breakfast, upon an empty stomach, and then four hours later allow the patient to eat as usual. The specimens of saliva and urine may, of course, be saved and all examined afterward.

Before drawing conclusions in regard to the intensity of the pancreatic digestion we must, of course, be sure that within six hours the capsules are dissolved neither by the gastric juice nor by any chemical agency in the intestine other than the pancreatic secretion. The author has proved that this is so by showing that these capsules can resist a strong gastric digestion for at least seven to eight hours, and the putrefactive changes in the intestine for twenty-four hours. When they are introduced, together with an Ewald test-breakfast, into a stomach with normal motility, they do not remain in the stomach much longer than one hour, but swell up in the gastric contents and are readily floated through the pylorus. Before a delayed reaction can properly be attributed to defective intestinal digestion the gastric motility must be tested and proved to be normal by withdrawal of a test-breakfast and lavage. For this no method of gastric examination is adequate in which the stomach-tube is not employed. If there be motor insufficiency of the stomach, a retarded reaction is to be ascribed to the delay of the capsule within the stomach, whether it has been dissolved there or, later on, in the intestine.

Individual differences in the rapidity of the excretion of the iodin and salicylic acid, in consideration of the test's duration, are not responsible for any considerable error in it because experiments have shown that, even in functional kidney affections, as soon as these substances get into the circulation the reaction appears in the saliva very quickly. On the contrary, another factor in the experiment is important, viz., the rapidity with which the iodoform is absorbed after the capsule has been dissolved by the pancreatic juice. The glutoid capsule test gives us, therefore, the resultant of the power of the pancreatic digestion and the absorptive power of the intestine. If we wish to determine the latter alone, we can repeat the test on another day, when we are sure that the saliva no longer gives an iodin reaction (nor the urine a salicyluric acid reaction), administering the iodoform (or salol) in an ordinary capsule with a glass of water on an empty stomach. From von Mehring's experiments it is fair to assume that under these conditions the stomach empties itself promptly into the duodenum and that thereby most of the salol and iodoform, despite the weight of the latter, is hurried along into the intestine by the rapid passage of the water. According to these experiments, moreover, absorption always occurs so rapidly (see above) that the results of the glutoid test depend almost entirely upon the sufficiency of pancreatic digestion, provided gastric motility be normal.

The results obtained from this method of examination are interesting. Even when the stomach-contents contained no free hydrochloric acid or pepsin, the reaction was not delayed so long as the gastric motility was good. The remarkably good state of nutrition of such patients, and the result of such a test, prove that the intestinal digestion may perform vicariously the entire gastric function. In cases of diarrhea, due only to an increased peristalsis, without any marked disturbance of intestinal digestion, the reaction is either normal or even somewhat hastened, on account of the favoring influence of increased motility. In other types of diarrhea characterized by an involvement of the intestinal chemistry or intestinal absorption, the reaction is either absent or distinctly delayed. In the latter case the

[1] It is evident that the patient should completely empty the bladder each time.

undigested capsules are often found in the feces, together with macroscopically visible undigested food-remnants. This method also aids in differentiating an icterus due to occlusion of the ductus choledochus at its point of entrance into the intestine from one where the obstruction to the bile flow is higher up, near the liver. In the former case the digestion of the capsules may be interfered with because the pancreatic duct is simultaneously plugged. Of course, the pancreas may have a separate exit of its own, besides the one in common with the choledochus. The test also aids in the diagnosis of pancreatic affections, *e. g.*, in several cases of carcinoma of the pancreas which the author has observed a negative result has supported a presumptive diagnosis of such a position for the tumor. Circumscribed carcinomata of the pancreas do not necessarily occlude the duct, however, so that, of course, a normal glutoid reaction will not exclude cancer of the pancreas.

Considering his estimation of the diagnostic value of the glutoid reaction mentioned above, the author is quite unable to understand how the assertion, copied from writer to writer, that the glutoid reaction possesses "merely a negative diagnostic value," can possibly be credited. From this presentation it is evident that if the reaction be critically carried out, *i. e.*, after considering and studying the gastric function and the intestinal motility (diarrhea), both negative and positive results furnish unquestionable conclusions in regard to normal as well as disturbed pancreatic function.

A. SCHMIDT'S TEST OF THE PROTEOLYTIC PANCREATIC FUNCTION—THE SO-CALLED NUCLEUS TEST

Schmidt starts with the fact (proved by himself) that cell nuclei are digested by the pancreatic juice, not in the stomach. He cites the following method of testing the pancreatic digestion: "Slightly marbled beef is cut into ½-centimeter cubes, which are hardened in absolute alcohol. These are then put into tiny bags of silk gauze, so that they may be easily recovered from the feces and set aside in alcohol. A few hours before use the bags are immersed in water. The patient swallows these bags upon several successive days during which he eats a definite diet. The bags are recovered from the feces by mixing the latter with water and straining. They are then washed, and their contents, which are chiefly muscle residue, are examined for nuclei after making fresh preparations with acetic acid and staining dry smears with methylene-blue. Schmidt found that complete preservation of the nuclei indicates an entire absence of pancreatic juice. If the pancreatic function be not completely lost, the nuclei may be digested. One source of error may be diarrhea, for then the bags may be so hurried through the intestine that the nuclei cannot be digested; another, the destruction of the nuclei by intestinal decomposition. This should occur only after a twenty-four-hour stay of the bags in the bowel, a circumstance which must frequently happen.

BOAS' AND VOLHARD-BOLDIREFF'S METHODS OF OBTAINING INTESTINAL JUICE

Boas[1] has shown that it is often possible, both in healthy and sick persons, to obtain enough duodenal secretion, consisting of pancreatic juice, bile, and succus entericus, for an examination. This method depends upon the fact that, as Boas and others have found, the pyloric closure can often be overcome easily by a very moderate straining, so that the duodenal contents enter the stomach. As the duodenum, like the fasting stomach, often contains preformed secretion, it is sometimes possible to force this into the stomach by the patient straining gently. The examiner can help a little by massage of the duodenal region. The technic of the procedure is as follows: The stomach-tube is first introduced, and whether or not the stomach be empty is determined by expression (see p. 442); if it be not, it is carefully washed with a 1 per cent. solution of sodium carbonate. With the patient in the dorsal decubitus, the region under the right costal arch, between the mammary and parasternal lines, is massaged from right to left for several minutes, and then, after the tube has been introduced, the patient expels the gastric contents in the ordinary way by the help of coughing or straining. With such a method we can often obtain 40 to 50 cc. of a neutral, alkaline, or weakly acid fluid. The acid reaction is due to the admixture of the preformed gastric juice which is usually present. The

[1] Boas, Ueber Darmsaftgewinnung beim Menschen, Centralbl. f. klin. Med., 1889, vol. x, No. 6, p. 97. The same, Zeit. f. klin. Med., 1890, vol. xvii, p. 155; also Tschelenoff, Ueber Darmsaftgewinnung beim Menschen, Correspondenzbl. f. Schweizer Aerzte, 1889, No. 6, p. 161.

fluid is usually stained strongly with bile. We can prove that it is duodenal by demonstrating a typical proteolytic, lipolytic, and diastatic action (see below).

Following Boldireff's physiologic experiments on dogs, Volhard[1] has shown that in man there occurs a regurgitation of pancreatic juice and bile into the stomach if an abundance of fat be ingested, and that with an oil breakfast it is possible to recover pancreatic juice, with or without bile from the stomach. He introduces 200 cc. of olive oil through a tube. One-half hour later he withdraws what remains, generally 50 to 100 cc. of oil, together with a watery, mucoid, often greenish fluid, which can be readily separated from it either by the use of a pipet or of a separating funnel. The advantage of this over the Boas method is perhaps that the pancreatic juice obtained in this way is more constant and probably of a physiologic character, corresponding to the stimulation employed. Volhard was able to demonstrate tryptic action in 86 per cent. of his cases by the casein method given below.

Although these procedures must not be considered as entirely irreproachable methods for testing the intestinal functions, because the conditions do not quite correspond to the physiologic requirements, nevertheless Boas' and the preferable method of Volhard may be depended upon to diagnose the presence of pancreatic action, *i. e.*, the patency of the pancreatic duct, just as well as the employment of glutoid capsules (p. 506). A quantitative estimation of the tryptic power of such an "oil juice" must be made with some caution because trypsin is obviously altered by the gastric juice and because a partial alteration cannot be excluded, since the "oil juice" has an acid reaction due to the admixed gastric juice. It would be interesting to determine whether the regurgitation of the pancreatic juice into the stomach in Volhard's method is to be considered a physiologic procedure conforming to the principle of adaptation (transference of the fat digestion to the stomach), or as a sort of pathologic appearance induced by fat ingestion. The demonstration of trypsin in the pancreatic juice obtained in this way is easy; but the demonstration of the lipolytic and of the diastatic enzymes has not yet been always successful. For examination, the fluid must, if necessary, be rendered distinctly alkaline as soon as possible by the addition of a weak sodium carbonate solution (so as to prevent any of the trypsin being destroyed by pepsin). Trypsin can be most easily demonstrated by digesting in the alkaline fluid, at incubator temperature, a flake of fibrin stained with Magdala-red. The fibrin, which is dissolved by the tryptic digestion process, colors the fluid red.

Arthus and Huber[2] have announced another method for demonstrating the action of trypsin. Fresh fibrin is prepared by whipping freshly drawn horse blood, and then washing the coagulum with water until it becomes colorless. It is finally completely covered and allowed to stand for twenty-four hours at 40° C., in a 2 per cent. solution of sodium fluorid, then filtered. We thus obtain a solution of fibrin in sodium fluorid which will keep for months. The fluid which is to be examined for trypsin is first diluted with an equal volume of a 2 per cent. solution of sodium fluorid, and one volume of this dilution is added to two or three volumes of the fibrin solution, and the whole mixture digested for a considerable time at 40° C. If trypsin be present in the fluid, crystals or crusts of tyrosin will form on the walls of the vessels. The crystals may often be recognized by the naked eye. In addition to their crystalline shape (see Fig. 240) they are characterized by their appearing light on a dark background in the polarizing microscope (with crossed prisms). One advantage of this procedure is that the digestive mixture remains sterile for an unlimited length of time, owing to the antiseptic qualities of the sodium fluorid.

For the qualitative as well as the quantitative testing of the tryptic action of the "oil juice" Volhard employs the alkaline casein solution, prepared for his method of estimating pepsin. (See p. 468.) He permits digestion in the mixture, which has been poured into two long-necked digestion flasks, like those in the method for estimating pepsin, and placed in the water-bath, and then proceeds in the same way as in pepsin estimations. After acidulating, he precipitates the undigested casein with sodium sulphate, filters, and titrates the filtrate. He then compares the acidity with that of the mixture which, save for digestion, has been similarly treated, and makes a proportion between the increase in acidity and the amount of the products of digestion. (See p. 468 et seq, for the principle of the method.) The technic is as follows: "100 cc. of the alkaline casein solution are measured off in two digestion flasks (see p. 468), chloroform water is added up to the 300 cc. mark; 5 cc. of the "oil juice test" are added to one flask, while the other serves as a control. Both flasks are placed in a water-bath; the temperature is kept at 40° C. by means of a toluol regulator, and the contents are allowed to digest for from one to twenty-four hours. Eleven cc. of normal HCl solution are then added to each flask until all

[1] Münch. med. Woch., 1907, No. 9. [2] Arch. de Physiol., 1894, p. 622.

the precipitated casein is again dissolved. The undigested casein is precipitated by the addition of a 20 per cent. solution of sodium sulphate, which is poured in nearly up to the 400 cc. mark. The mixture is then shaken, and after cooling, brought exactly to 400 cc. by the addition of more sulphate solution. It is then filtered into a measuring glass, and 200 cc. of the filtrate are titrated against phenolphthalein with $\frac{N}{10}$ or $\frac{N}{4}$ sodic hydroxid solution. The difference in acidity of the two filtrates gives a measure of the tryptic action." By this method Volhard found that the Schütz-Huppert law of geometric proportion cannot be applied to trypsin digestion (see p. 469); but rather a law of arithmetic proportion. The amount of the digestive products are proportional to the amount of juice employed, so that if the increase in acidity of the filtrate in the procedure be represented by a, and the amount of juice by j, the fraction $\frac{a}{j}$ is a constant. Müller serum plates (see p. 542) may also be employed to demonstrate tryptic action.

Grützner-Gamugee recommended the following method to demonstrate lipolytic activity: An emulsion of 10 parts of oil, 5 parts of gum, and 35 parts of water is prepared; also a neutral solution of litmus, which, in test-tubes of 12 mm. diameter, appears violet against white paper. Ten cubic centimeters of such a litmus solution and 5 drops of the emulsion are placed in several of these tubes; and increasing quantities (*e. g.*, 2, 4, 8, 16, and 32 drops) of the fluid to be examined are added to the successive test-tubes. They are then immediately set in a water-bath at 37° C. After a few moments the different tubes are compared. If any fat-splitting ferment be present, the color of the fluid will have turned redder the larger the amount of solution added. For further tests see Hammarsten's Text-book of Physiologic Chemistry, translated by Mandel, fifth edition, 1908, p. 389 et seq.

To demonstrate diastatic action, increasing amounts of the fluid to be examined are added to a thin starch paste. If a minimal amount of iodin be then added to this mixture and no violet color appears (see p. 448), we obtain evidence that a diastatic action has taken place. Again, the presence of dextrose, as shown by Trommer's test, will prove the same thing. (See p. 587 et seq.) Müller's starch paste tablets (see p. 542) may also be used.

EXAMINATION OF THE FECES[1]

Introduction.—The author emphasizes the necessity for the patient's coöperation, and urges the general use of water-closets of such construction that the stools can be readily observed by the patient.

FREQUENCY OF MOVEMENTS; DIARRHEA; CONSTIPATION; AMOUNT OF FECES

There is considerable variation in the *frequency of the bowel movements* even in health. Some absolutely healthy people have a movement of the bowels only once in two or three days, others have several every day. There is no sharp line of distinction in either direction between the pathologic and physiologic. The term constipation is usually restricted to a condition of infrequent movements which is associated with certain other difficulties or which does not bear a proper relation to the quantity of food taken; in the same way the term diarrhea is employed only when the movements are not only frequent, but also liquid. Infants normally have two or three movements in twenty-four hours.

Other things being equal, the frequency of the movements depends upon the amount of nourishment ingested. In starving individuals the number is reduced to a minimum; and in many and most varied diseases a more or less complete state of starvation may be developed. For instance, an individual who vomits everything is practically starving. In the same way a gastric case or any other person severely ill

[1] Consult J. Schmidt and J. Strassburger, Die Fäces des Menschen, Berlin, Hirschwald, 1901.

who takes little on account of lack of appetite or because he cannot retain anything, is to be considered as a case of starvation.

Diseases which give rise to *constipation* are: gastric and intestinal catarrh (especially chronic), gastric dilatation, intestinal obstruction of various sorts, peritonitis, meningitis, and other diseases which increase the cerebral pressure. Sometimes constipation becomes a more or less independent malady (chronic constipation), which is referable to a great variety of causes.

A complete absence of movements is generally characteristic of some kind of intestinal obstruction. Not infrequently, however, fecal material may be evacuated for some time from the section of the intestine below the obstruction. Continuous diarrhea is characteristic of some types of obstruction, especially of invaginations, of incomplete axis rotations, or of certain strangulations. But these movements are really not fecal in character; they consist of serous or, often, bloody masses from the lower intestinal segment, due to the venous congestion at the seat of lesion. Their character and sometimes the absence of the passage of gas which is in marked contrast to the presence of formed or fluid movements should be sufficient to justify the diagnosis of obstruction.

Diarrhea occurs in acute and chronic gastric and intestinal catarrh, in certain types of chronic peritonitis, in intestinal tuberculosis, intestinal amyloid degeneration, cirrhosis of the liver, cholera, typhoid fever, dysentery, many other infectious diseases, and uremia.

The daily quantity of the feces passed, other things being equal, is directly proportional to the amount of food ingested. The volume of the individual movements is generally inversely proportional to the number.

There are, however, numerous exceptions to the last two statements, *e. g.*, in patients who vomit, often much less is evacuated in the movements than is ingested. Again, in severe forms of diarrhea, especially cholera, much more is evacuated than is ingested, because, in addition to the food residue, there are the secretions and exfoliation of the intestinal mucous membrane. The admixture of blood may also increase the quantity of the feces.

In diarrhea the individual movements vary in volume and frequency according to whether the disease is localized in the upper or lower intestine. In diseases of the lower part of the colon, of which dysentery is a type (rectal diarrhea), the individual evacuations are not very voluminous, but they are very frequent, on account of the continuous reflex tenesmus. In diseases of the upper intestine each evacuation is more profuse, but they do not occur so frequently (*e. g.*, typhoid), because there is not the same persistent desire to empty the rectum. These, so to speak, "profuse" diarrheas may be found in involvement of the upper portion of the colon as well as of the small intestine.

After a period of marked constipation quite incredible quantities of feces are often passed.

CONSISTENCE AND SHAPE OF FECES; STRATIFICATION OF LIQUID MOVEMENTS

The normal consistence and shape of feces is well known. The consistence is hard in constipation, fluid in diarrhea. Between these extremes are all sorts of intermediate forms. The small fecal balls, like sheep dung, which occur in intense constipation, from the tightly packed fecal matter becoming friable, are especially noteworthy. On the other hand, scybala may be of very unusual volume in constipation if a large quantity of feces stagnate in the rectum and distend it mechanically.

In intestinal stenosis but a short way above the anus the fecal masses have a diminished transverse diameter; but if the stenosis be high up, their shape changes again below the obstruction. Leichtenstern has justly called attention to the fact that a similar small caliber of the fecal masses may be found also in inanition (starvation feces) and in tenesmus (spasm of sphincter).

Very liquid diarrheal movements often stratify themselves with the liquid constituents in an upper layer, and the solid food residue in the lower. Frequently, however, the formation of layers is due simply to an admixture with urine.

COLOR AND GENERAL APPEARANCE OF THE STOOLS

The normal color of the stools of an adult is dark brown. This color is not due to biliary pigment, but to its secondary products (urobilin, etc.). Infants' stools are normally light yellow or golden yellow, because they contain unaltered bilirubin.

The color of the feces varies more or less according to the nature of the food. A milk diet and much fat gives a light color to the stools; abundant consumption of red wine, blueberries, blackberries, or black cherries, on the other hand, gives them a dark color. Food rich in chlorophyll (vegetables) may, under certain conditions, produce a green or olive shade in the stool. The ingestion of chocolate, and especially of cocoa, causes a noticeable red-brown color. Drugs may also change the color of the feces. Extract of logwood produces a reddish-brown color in the stools. After the employment of rhubarb, senna, santonin, and gamboge, a very pronounced yellowish-brown color is observed. If the stool be alkaline, or if alkali be added, the shade is more nearly red. Calomel is apt to color the stools greenish. According to Wassilieff and Hoppe-Seyler, this coloration is not due to the formation of sulphur compounds of mercury, as was formerly believed, but to the antiseptic action of the calomel, which inhibits the transformation of the bile-pigments into urobilin, and also to the sublimate derived from the calomel, which changes the bilirubin to biliverdin. (See p. 575.) After the use of bismuth the stools are generally of a blackish color. Quincke [1] has proved that this color is not due to the formation of metallic sulphur, as was formerly thought to be the case, but rather to a reduction of the bismuth salt to bismuth suboxid, as in Nylander's test for sugar. Not infrequently bismuth stools are colored green, very much like those after calomel, a phenomenon which Quincke explains by assuming that the bismuth also checks the transformation of the bile-pigments to urobilin. He claims that, contrary to the general belief, the stools after the use of iron are not black from ferrous sulphate. He maintains that immediately after evacuation they present no abnormal color, and certainly not black, but become grayish brown to grayish black only after standing and only upon the surface exposed to the air. He believes that this phenomenon is due to the oxidation of organic iron combinations when exposed to the air. Patients to whom we administer iron are usually the ones in whose dark-colored stools there is often an admixture of blood. If these statements be heeded, it is generally easy enough to distinguish bloody stools from those containing iron. Yet the author has observed a case of icterus with complete obstruction of the common duct in which the stools, as a result of a chemically demonstrable admixture of altered blood, exhibited a peculiar dark-gray color like graphite. The character of the stools after the administration of methylene-blue gives evidence of the processes of reduction going on in the intestinal canal itself. When freely evacuated, they are usually of the ordinary color, due to the reduction of the methylene-blue, but within a few moments they become bluish green on the surface. This coloration gradually penetrates the mass. If the stool be preserved under oil, no such color appears.

Chromogenic bacteria may also produce an abnormal color in the stools. Bacteria producing green pigment have been found in the stools of small children (Lesage). The author has seen a marked violet coloration of the stool, due to a profuse growth of Bacillus pyocyaneus. He was able to extract the pigment in large amounts and to establish its chemical identity.[2]

[1] Münch. med. Woch., 1896, No. 36.

[2] See H. Girard, Zeit. f. Chir., vol. vii, in regard to the characteristics of pyocyanin.

Under pathologic conditions the stool may be abnormally colored by the addition of blood. (See p. 514 et seq.) The stool is abnormally light in color in *acholia* (deficient production of bile with absence of icterus) and in retention of bile due to occlusion of the biliary passages (in icterus). Such stools present a peculiar grayish-white appearance (clay-colored). This is due not only to the deficiency in amount of bile, but also to an abundance of unabsorbed fat.

Nothnagel[1] distinguishes uncolored feces from acholic stools. The former occur not only without any icterus, but, in contradistinction to the latter, without any demonstrable disturbance of fat-absorption. Nothnagel and von Jaksch suspect that in these cases, instead of urobilin, colorless reduction products are formed in the intestine from bilirubin (Nencki's leucourobilin, urobilinogen). This subject has not as yet been very closely studied from a chemical standpoint. Nevertheless, this possibility is certainly suggested, because von Jaksch succeeded in extracting with acid alcohol very considerable quantities of urobilin from such so-called acholic stools (see p. 583), and because such stools often darken considerably when exposed to the air, an effect evidently to be ascribed to oxidation. This may be termed pseudoacholic. Quincke claims that the normal color of such stools is reproduced when calomel is administered, merely because the latter inhibits the reduction of the urobilin, which is ordinarily caused by putrefactive processes in the intestine.

In diarrhea the movements are, generally speaking, light colored, because the pigment is distributed through a much larger volume, but sometimes (especially in intestinal catarrhs) they may contain the bile-pigment and vary in color from green to yellow. (See p. 575 et seq. for the demonstration of bile-pigment in the stools.) The presence of unchanged bile-pigments in the stools is always pathologic, except in infants (see above).

We sometimes find undigested food-particles in the stools. This is of no diagnostic significance so far as indigestible constituents are concerned, such as seeds, stones, and the skins of fruits. But if the stools contain considerable macroscopic evidence of substances which are ordinarily so changed by the intestinal digestion as not to be recognized (*e. g.*, bits of meat, flakes of casein, etc.), we naturally attribute this peculiarity to some digestive disturbance. This condition, found in stomach and intestinal disorders, was formerly described as "lientery." If there be a fistulous communication between the stomach and intestine or between a loop of the upper and a loop of the lower intestine, more or less undigested food will appear in the stools. (See p. 529 et seq. for the microscopic examination of the stool with reference to the assimilation of the food.) If excessive decomposition processes take place in the intestine, the diarrheal movements will exhibit a peculiar foamy character. In infantile diarrhea the stools are often of a greenish color, due to the abnormal decomposition of the bile-pigment: or if there be many flakes of undigested casein, they may have a granular or lumpy instead of their normal smooth appearance.

With reference to the admixture of mucus, blood, and pus in the stools, see the following pages.

ODOR OF THE STOOLS

The odor of normal human feces is well known. It is due chiefly to indol and skatol, and perhaps also to methyl mercaptan. The fecal odor is much more pronounced upon a meat than upon a vegetable diet.

[1] Die Erkrankungen des Darmes und Peritoneums, p. 18.

The normal stool of an infant emits only a very faint odor, which is not peculiarly fecal. In intestinal catarrh, however, the odor of infants' stools may be very foul. The odor of diarrheal movements varies greatly, sometimes abnormally strong, sometimes noticeably slight. The thin stools of cholera are particularly lacking in odor. Nearly odorless stools very frequently follow the use of strong cathartics. The presence of volatile fatty acids in certain types of diarrhea may be responsible for a sour odor to the stools. Abundant admixture of mucus sometimes gives the stool an odor like semen. Boas has observed the odor of lime in amebic dysentery. (Compare the characteristics of certain types of stools on p. 540 et seq.)

VISIBLE ADMIXTURE OF MUCUS IN THE STOOLS

A noticeable admixture of mucus in the stool will be recognized here, as in other excreta, usually by its peculiar consistence and transparency. In a doubtful case the addition of dilute acetic acid will cloud the portions containing mucus. The mucus in the feces is a true mucin.

Even a normal stool contains some mucus, which is, however, usually only demonstrable chemically. In quite solid feces this normal mucus may adhere to the surface of the stool in the form of visible clumps. Greater amounts of mucus indicate some catarrhal condition of the intestinal mucous membrane.

In catarrh of the small intestine the mucus is evenly distributed in the solid or semisolid feces, and may be recognized by the slimy consistence of the whole stool or by the presence of small, evenly distributed shreds or tiny transparent lumps. We must, however, be careful not to confuse bits of swollen vegetable tissue, especially from fruit, with lumps of mucus. The former are frequently found in a normal stool, and can be easily recognized microscopically by their cellular structure. (See Fig. 201*a*, p. 428.) Large shreds of mucus in thin stools are found, especially in catarrh of the large intestine. The large lumps of mucus which sometimes coat scybala also result from catarrh of the colon. Frequently a marked ileus produces similar collections of normal intestinal mucus. Mucous stools interspersed between normal movements are also observed in catarrh of the large intestine in colica mucosa, which is not yet clearly understood, and in the affection which some writers differentiate from it, viz., enteritis membranacea. These peculiar whitish, ribbon- or tube-like formations are passed frequently with severe colicky pains, probably due to the violent peristalsis needed to tear them from the wall of the large intestine. The laity often mistake these formations for tape-worm. An admixture of mucus in small shreds is observed in the otherwise almost purely watery stools of cholera (rice-water stools, see p. 540. With reference to the chemical test for mucin, see p. 543).

VISIBLE ADMIXTURE OF BLOOD IN THE STOOL

The blood contained in the stool may exhibit itself in different ways. Sometimes a microscope is required to demonstrate it; at others it may be recognized macroscopically by a red or blackish color. (See next page in regard to the dark-gray color of acholic stools produced by admixture of blood.)

Various deductions in regard to the seat of the hemorrhage may

be made from the color and distribution of the blood admixture. For instance, solid feces coated externally with blood would indicate a hemorrhage only in the lower portion of the intestine, where the feces are already solid and formed (hemorrhoids). Conversely, solid feces evenly tinged throughout would point toward a hemorrhage in the stomach or the upper part of the intestine. Even in liquid stools the admixture of blood is usually more intimate if the hemorrhage be in the upper part of the intestine. But the liquid movements from the large intestine (dysenteric meat-juice stools, see p. 540) may also contain evenly mixed blood. The color of the blood in liquid stools sometimes forms a good criterion for determining the seat of hemorrhage. The higher the hemorrhage is, the more altered is the original blood color, due to intestinal putrefaction and intestinal digestion (transformation of the hemoglobin to methemoglobin and hematin). In hemorrhage from the stomach, gastric digestion may also cause some change. Profuse hemorrhage from the stomach does not always cause hematemesis, so that we may first suspect the condition from the appearance of the stools, which may be nearly black and of a tar-like consistence. Profuse typhoid hemorrhages sometimes show an alteration of the blood; usually, however, it is still distinctly red, because it generally comes from the ileum, and a stool follows a hemorrhage quickly. The bloody, serous diarrheal stools without true fecal matter are of great diagnostic importance in certain types of ileus, especially invagination. (See p. 511.) (See p. 540 for other peculiarities of certain diseases characterized by blood in the stools.)

The diagnosis of obscure cases of carcinoma and of ulcer of the stomach and intestines has been materially assisted by the demonstration of so-called *occult* hemorrhages, *i. e.*, the slight but generally constant admixture of a very small amount of blood demonstrable only by chemical test. Boas has recently emphasized the importance of this occurrence. In the color of the stool there is often nothing peculiar. The author once saw a case of icterus due to carcinoma of the gall-bladder where occult blood was always present in the acholic stools which exhibited a pale, graphite-like color without a suggestion of a tinge of blood.

In doubtful cases a microscopic examination may determine the presence of blood in the feces; but the red blood-corpuscles are often found considerably changed and hard to recognize. Sometimes they may be destroyed completely, and then the question as to whether or not blood is present must be decided by a chemical or spectroscopic examination. (See p. 544 et seq.)

PUS IN THE STOOL

Conclusions similar to those discussed under blood in the stools may be drawn from the different ways in which pus is mixed with the fecal material. A very considerable admixture of pus or pure pus stools are always due to perforating abscesses. A slight amount of pus in the stool, which often can be demonstrated only microscopically (polynuclear leukocytes), and which is frequently associated with blood or mucus, may be due to catarrhal changes, but is generally due to ulcerative processes of the mucous membrane (tuberculosis, dysentery, etc.). Lumps of pus indicate an ulcerative process. It may be very difficult to demonstrate pus in the stool, because the pus-corpuscles are sometimes destroyed by duodenal digestion and putrefaction in the colon.

Experiments bearing directly on this point have convinced the author that intestinal decomposition may destroy pus-corpuscles within a comparatively short time, so that it is impossible to recognize them. The polymorphous nuclei may resist the decomposition for a considerable length of time, but they are difficult to recognize in this isolated condition, especially as they break into fragments so readily and differ in no way from the cell nuclei of any animal food, which may persist after digestion. Moreover, even in normal stools individual polynuclear leukocytes may be found as a result of the normal transmigration through the mucous membrane. The demonstration of pus is sometimes difficult, even in perforation of perityphlitic abscesses into the intestine, because decomposition in the abscess has already begun to change the character of the pus, and this change is still greater in the colon.

The undigested lumps of casein found in the diarrheal movements during a milk diet must not be confounded with shreds of pus. Although impregnated with fecal pigment, the former sometimes assume a pus-like appearance; they may easily be recognized microscopically by the fat-drops which they contain.

TUMOR FRAGMENTS IN THE STOOL

Larger or smaller pieces of tumor are not infrequently cast off in carcinoma of the rectum or of the intestine higher up. These fragments attract attention chiefly in a liquid stool by their grayish-red color and solid consistence.[1]

As it is often impossible to recognize the finer details on account of putrefaction, the essential point is to detect the numerous nuclei arranged according to the character of the cell constituents and without the cellular membranes of vegetable cells, which latter usually resist putrefaction. Fragments of adenomatous polyps are sometimes found in the stools. They may occur independently or they may be located in the neighborhood of carcinomatous and tuberculous ulcers of the intestines.

CONCRETIONS IN THE STOOLS

GALL-STONES, PSEUDO-GALL-STONES, BILIARY GRAVEL, PANCREATIC STONES, INTESTINAL CONCRETIONS, INTESTINAL SAND, MEDICINAL CONCRETIONS

In cholelithiasis an attack of biliary colic may be followed by the appearance of gall-stones from time to time in the stools, or they may appear without any previous biliary colic. In searching for them the stool should be thoroughly mixed with water and washed and rubbed through a sieve. The Boas stool sieve[2] is very convenient; it is supplied with a water connection and washes the stools automatically. To be certain, we should examine the stools during at least fourteen days after the cessation of the attack of colic.

Gall-stones are concretions which form in the biliary passages, from the size of a pinhead to that of a pigeon's egg, or even larger. They consist chiefly of cholesterin and calcium bilirubin, in varying proportions and sometimes chiefly of one of these constituents. Besides these there are present minor amounts of biliverdin,

[1] A bit may be teased apart or, better, frozen and sectioned and then examined microscopically, or the fragments may be placed in a 4 per cent. watery solution of formaldehyd (℞. Formaldehyd solution venale (40 per cent.) 100, aq. dest. ad 1000). Bits of from 0.5 to 1 mm. in thickness are sufficiently hardened after one-half to two hours; but it does no harm to leave them in the solution up to eight days. The pieces are then frozen either with the formalin solution itself or with water and cut; the sections are placed in 50 per cent. alcohol and stained with aqueous anilin dyes. By this method the sections are said to be much better preserved than with the ordinary freezing process.

[2] Deut. med. Woch., 1900, No. 36.

bilicyanin, bilifuchsin, bilihumin, and calcium carbonate. Cholesterin gives a light, and calcium bilirubin a dark, color to the concretion. The color varies according to the predominance of one or the other of these constituents, between white and dark brown or dark olive green. Sometimes they are soft enough to be readily cut or crushed, but often, on the contrary, are rather hard. The cross-section usually shows distinct concentric layers of crystalline structure, sometimes of different colors. In other cases the surface may present very beautiful facet formations, so that tetrahedra and cubes or multiangular shapes result. Sometimes the surface is irregularly granular, a point of diagnostic importance. If facets be numerous and distinctly shaped, we may be sure of the presence of multiple concretions, and, in all probability, of their origin in the gall-bladder. Round stones occur singly and also in numbers. Very large stones (larger than hazelnuts) hardly ever reach the intestine *per vias naturales*, but probably always by perforation of the bile-passages into the bowel.

We must be careful not to confound other solid residues of the feces with gall-stones, *e. g.*, woody bits of plants, especially from the cores of pears. Such formations have been termed *pseudo-gall-stones*.[1] Microscopic examination of a small fragment scratched off with a knife from such a formation shows characteristic wood-cells (Fig. 212). Chemical examination (see below) would also prevent any mistake. Besides, the wood-like particles are much harder than even the hardest gall-stones.

Fig. 212.—Wood-cell from the seed of a pear (after Bizzozero).

So-called "*biliary sand or gravel*," in the majority of cases, consists of these small pseudo-gall-stones. Perhaps the occurrence of intestinal sand or gravel (see p. 518) has been responsible for the erroneous assumption of biliary sand. The existence of true biliary sand (*i. e.*, large numbers of the smallest gall-stones) in the feces has not been surely proved as yet. Naunyn considers it improbable, because his investigations show that these small concretions are readily dissolved in the intestine, and because they would not be passed in any such large quantities at one time, but gradually, as they were formed.

Another kind of pseudo-gall-stones is the concretion which consists of fats and fatty soaps that are not easily melted. They are found in the stools after the administration of large amounts of olive oil in treating cholelithiasis. Hence, the overestimation of the therapeutic value of this oil. It is difficult to understand this error. These artificially produced concretions are characterized usually by their transparency and soft, greasy consistence, and, if the biliary passages be not occluded, by their greenish color, due to impregnation with bile.

Even a careful and prolonged search may fail to find the concretion in certain cases of *gall-stone disease*, sometimes because the stone, which was impacted in the neck of the gall-bladder and so caused the colic, has returned to the bladder itself. In other cases the stones which are at fault have become stuck in the ductus choledochus while the patency of the biliary passage has been reëstablished without dislodgment of the stone. Finally, the concretion may be disintegrated in the bowel and so escape detection. Naunyn's experimental investigations seem to prove that the latter is very often the case. He believes that ordinarily only the more solid gall-stones (for instance, those with a solid cholesterin shell) are found in the feces. Another explanation of the cases where no gall-stone is found in the feces after the typical symptom-complex of cholelithiasis is the following: typical attacks of colic may be due to inflammation with or without gall-stone. Numerous experiments have disproved the old idea that the colic arose mechanically by the passage of the stone through narrow places of the ducts. These experiments show that an inflammation of the bile-passage and a resulting spasmodic peristalsis are the essential features of a gall-stone attack, and that a typical picture of such an attack may occur without the presence of a gall-stone.

[1] Compare Fürbringer, Verhandl. d. XI. Cong. f. inn. Med., 1892, p. 313.

For *chemical examination* gall-stones are first dried, then powdered, and then extracted with alcoholic ether to dissolve the cholesterin. This may be easily recognized by allowing the solution to evaporate slowly in a watch-glass. The characteristic glistening cholesterin crystals separate, and are easily recognized under the microscope by their sharp, linear, rhombic outline. (See Fig. 278.) After extraction with alcohol and ether the residue is washed and then treated while cold with very dilute potassium hydroxid. If the powder contain calcium bilirubin, we get a yellow solution, with which Gmelin's reaction may be obtained (p. 575). Naunyn claims that some concretions contain only bilihumin, in which case the green in Gmelin's reaction will be absent and only the blue ring will be found. The residue after treatment with KOH is, for the most part, soluble in HCl. If Ca_2CO_3 be present, solution is accompanied by effervescence.

The much rarer *pancreatic concretions* differ from gall-stones in not containing bile coloring-matter, and, chemically, in consisting chiefly of calcium carbonate, which dissolves with effervescence in hydrochloric acid. They seldom have facets.

Intestinal Stones or Fecal Concretions; Earthy Concretions; Incrustations of Food-particles with Organic Salts.—These play an important part in human pathology as excitants of appendicitis. They appear very rarely in the stools. They consist almost exclusively of ammonium and magnesium phosphate, and should be examined in the same way as urinary calculi. (See p. 680.) Eichhorst and Deetz [1] report cases, which were not sufficiently explained pathologically, in which large quantities of intestinal sand, consisting of finely granular mineral concretions, were passed in periodic attacks. Perhaps these cases have at times been erroneously considered of biliary origin. (See p. 517.)

Some concretions found in the stools consist of materials taken by mouth, *e. g.*, concretions of magnesium carbonate and phosphate after the administration of magnesium carbonate, and combinations of bismuth after the ingestion of bismuth subnitrate. Salol is also a well-known cause of the formation of intestinal stones. Naunyn observed the passage of concretions of myrrh, rosin, and of rhatany tannate after ten years' use of the tincture of rhatany and myrrh. The occurrence of shellac concretions is well known in joiners and hatmakers, who sometimes employ the alcoholic solutions of shellac as drinks. In the same category (see p. 517) belong the "pseudo-gall-stones" consisting of fat which appear in the stools after the so-called oil cures.

ANIMAL PARASITES IN THE STOOLS

PROTOZOA

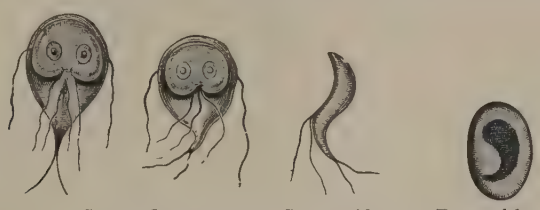
Of the protozoa, there have been observed in the human intestinal contents amebæ (Fig. 215), sporozoa of the species Coccidium (psorosperms), flagella of the species Megastomum (Fig. 214), Cercomonas (Fig. 213), and Trichomonas (Fig. 216), and infusoria of the species Balantidium. Except the last named, which sometimes penetrates the intestinal wall and so causes perforation,[2] these, so far as is

Fig. 213.—Cercomonas hominis: Length, 9 to 11μ; width, 5μ (Davaine) (after Roos).

known to-day, possess no definite diagnostic significance. In gastric and esophageal contents, on the other hand (see p. 431), they have been observed especially in carcinoma. Cohnheim and Zabel have observed that the settling of these parasites in the esophagus and stomach favors their appearance in the feces, hence their demonstration suggests, under some circumstances, the existence of gastric or esophageal

[1] Arch. f. klin. Med., vol. lxx, parts 3 and 4, p. 365.
[2] Askanazy, Wien. med. Woch., 1903, No. 3.

carcinoma. The parasites of the species Ameba have become of more importance recently, because they are supposed to be the cause of dysenteric-like disturbances (Fig. 215). Amebæ are organisms with streaming, creeping (so-called ameboid) movements. They are 10 to 15μ in diameter, and consist of a protoplasmic substance, containing granules and vacuoles, which changes its shape in an irregular way during the movements. Each ameba has a nucleus within it, which is, however, not always easy to see. Propagation takes place by division; the formation of spores has not been definitely proved. Some amebæ have permanent types (permanent cysts, encysted amebæ). These are small, round, with a sharp, often double, con-



Seen on flat. Seen on side. Encysted form.

Fig. 214.—Megastoma entericum: Length, 15 to 17μ; breadth, 9 to 11μ (after Roos Deut. Arch. f. klin. Med., vol. li, p. 506).

tour, and are immobile. The death of an ameba is indicated by the cessation of its ameboid movements (Fig. 215), and the organism then disintegrates so rapidly that it is not easily recognized. Quincke claims that the permanent types, on the contrary, may remain visible in the stool for twenty days.[1] Pure cultures have not yet been successfully made, so that it is difficult to obtain any light on the species of the individuals found.[2] Amebæ are sometimes found in normal intestinal contents. Large numbers are found quite regularly in tropical dysentery. Streptococci are also very frequently found in dysenteric stools along with the amebæ, so that some cases are probably due to mixed infection. The amebæ penetrate the

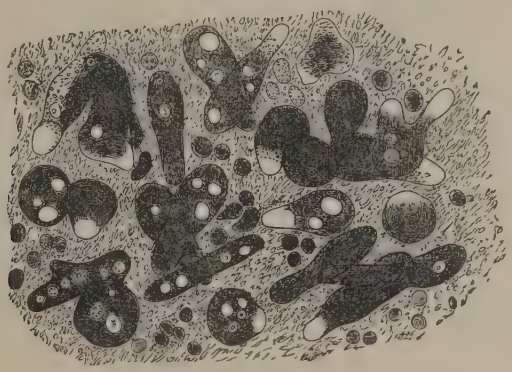


Fig. 215.—Amebæ of dysentery (after Lösch).

base of intestinal ulcers, and are also found in the pus of dysenteric abscesses, which speaks for their etiologic significance in tropical dysentery. In isolated cases of the common, non-epidemic dysentery amebæ have been found (Quincke), which, in contrast to the amebæ of tropical dysentery, are not pathogenic for cats. Quincke recommends the following nomenclature: *Amœba intestinalis vulgaris* for the organism which is sometimes found in the stools of healthy individuals; *Amœba coli*

[1] Quincke and Roos, Berlin. klin. Woch., 1893, No. 45; Janowsky, Zeit. f. klin. Med., 1897, xxxii, 5 and 6; Roos, Arch. f. klin. Med., vol. li.

[2] See Schaudinn, Untersuchung. über die Fortpflanzung einiger Rhizopoden, from the Kais. Gesundheitsamte, 1903, vol. xix, part 3.

(Fig. 215), the name used by its discoverer, Lösch, for the ameba of tropical dysentery[1]; and, half-way between these two, *Amœba coli mitis* for the above-mentioned parasite accompanying the common form of the disease. We do not really know whether these are different species or whether they are varieties of varying virulence.

The organisms can be most readily recognized by their ameboid motion, so that it is very important to examine the stool when freshly voided and contained in a vessel which has been warmed to 40° C. Bloody or purulent flakes are selected from the stool and examined microscopically. More solid masses must first be

Fig. 216.—Trichomonas intestinalis (Marchand): Length, without tail, 11 to 15 μ; width, 5.5 to 8 μ (after Roos).

diluted with warm physiologic salt solution. The motility of the amebæ can be preserved by employing a warm stage. The warm movable stage, constructed according to the author's directions by Leitz, in Wetzlar, is illustrated in Fig. 217. It is a combination of Schulze's warm stage, with a superimposed movable stage. The apparatus is attached to the stage of the microscope by two screws, which are not visible in the figure, and the stage is heated by two small burners beneath the points *a* and *b*. [Specimens for examination are best obtained by passing a soft catheter into the rectum or by detaching bits of mucus with an applicator after

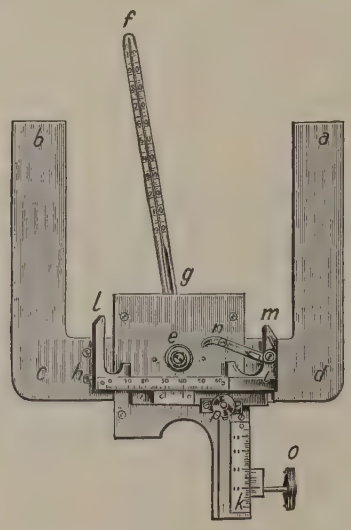


Fig. 217.—A movable stage which can be heated.[2]

passing a proctoscope. The mucus must be examined while warm and upon a warm stage. Swollen epithelial cells must be distinguished from the amebæ.—Ed.]

The living amebæ may be stained with a dilute solution of methylene-blue (1 : 20,000) or neutral red. In dry preparations their pale color makes a striking contrast to the deeply stained bacteria. For permanent specimens von Prowazek recommends spreading the mucus as thin as possible upon a cover-glass, and overlying

[1] In the common form, occurring in epidemics, the Krause dysentery bacillus seems to be the causative organism.

[2] Manufactured by Leitz, Wetzlar, from the author's design.

it while it is still moist with a steaming hot mixture composed of 100 cc. of concentrated aqueous sublimate solution, 50 cc. absolute alcohol, 5 cc. glacial acetic acid, allowing it to stand for one-quarter hour, then washing in water, extracting the sublimate with a pale-yellow solution of iodin, and staining with a dilute solution of Grenacher's hematoxylin. After staining the specimen should be washed in water until no blue color is noticeable in the wash-water, cleared with alcohol and xylol, and embedded in Canada balsam.

Enthelmintha (Intestinal Worms)

Discovering the eggs of one of the intestinal worms is almost as important, from the diagnostic point of view, as discovering the organism itself. A low power is the best to employ at first, and then a higher one. The stools should either be liquid or mixed with water. It is often sufficient to scratch off particles of feces from the edge of the anal opening with a microscope spatula, or to obtain some from the rectum by introducing the finger protected by a rubber cot. The Oxyuris vermicularis is not infrequently discovered in this way. Larger quantities of feces may be obtained by introducing a thick glass tube with blunt edges (Quincke). If the eggs cannot be demonstrated upon the first examination, administering some cathartic (castor oil) will often prove of service, probably because the liquid intestinal contents will thus be more evenly mixed. (For the characteristic peculiarities of the eggs of the different species see below.)

If neither eggs nor bits of the parasite be found after the administration of an ordinary cathartic, the next procedure is to give the patient some anthelmintic, *e. g.*, santonin. In case of ascarides this will serve the double purpose of diagnosis and treatment; but for tape-worm it is inadvisable because the drugs may do harm and should be administered only when necessary. In such a case the diagnostic dose should be very moderate—about one-third of the usual therapeutic dose, *e. g.*, 3 gm. extractum filicis. If a tape-worm be present, segments will then certainly be passed. In the interest of the patient too much stress cannot be placed upon the advisability of making an accurate diagnosis (segments of worms or eggs) before undertaking the actual cure.

Leichtenstern[1] has drawn attention to the diagnostic importance of Charcot's crystals in the stool (see Fig. 278, *e*, p. 707) for the recognition of intestinal worms. These crystals occur in the feces with every variety of entozoa, and often in very large amounts. They are often very small and require an oil-immersion lens for identification. Their relation to the presence of worms is not yet plain.

See Blood Examination with reference to the almost constant occurrence of Charcot's crystals and eosinophilic leukocytosis in the various types of helminthiasis.

Nematodes (Round-worms)

Ascaris Lumbricoides.—This is the only ascaris which occurs frequently in the human intestine (Fig. 218). The diagnosis of ascaris is generally very easily made, either from the eggs or from the worms themselves. The latter are 10 to 15 cm. long, white to dirty brown in color. They are almost always evacuated with the feces from time to time, and sometimes may be vomited. The ascarides eggs are passed in such great numbers with the feces that the examination of bits of feces from about the anal orifice is usually sufficient. They differ from all other entozoa eggs in their peculiar, irregularly wavy, albuminous shell, usually stained with feces. (See Fig. 218, *c*.) This envelop may, however, be absent. The longest diameter of

[1] Deut. med. Woch., 1892, p. 582.

the eggs is about 0.05 to 0.06 mm. The eggs often appear almost round (vertical position). Infection occurs from swallowing eggs containing embryos without an intermediate host (Lutz).

Ascaris mystax (**A. canis**) attain but a third the size of the Ascaris lumbricoides. They are recognized by two characteristic wing-shaped chitinous appendages at each side of the head, presenting an arrow-head appearance. They are common inhabitants of the intestines of cats and dogs, and are only rarely observed in man. Their eggs are spheric, finely granular.

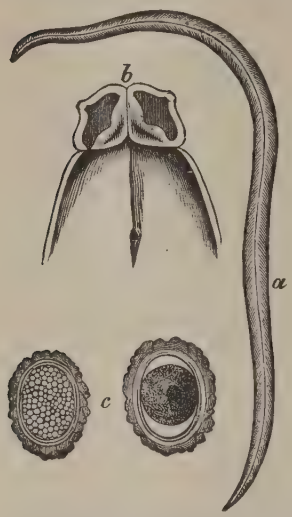


Fig. 218.—Ascaris lumbricoides: *a*, Body; *b*, head; *c*, eggs (after von Jaksch).

Oxyuris vermicularis (Fig. 219).—This small intestinal worm inhabits chiefly (but not exclusively) the large intestine as far as the cecum. It is 3 to 12 mm. long. It causes very annoying itching in the anal region, and should be searched for in almost any case of pruritus ani. Either the small thread-like worms are found in the feces or on the skin in the vicinity of the anus, or else the eggs are found microscopically in the bits of feces which adhere to the anal orifice. The eggs are 0.05 mm. long, and somewhat asymmetric in contradistinction to others. Leichtenstern has proved that oxyuris never lay eggs in the intestine, but always migrate through the anal orifice for that purpose. Hence for diagnostic purposes it is of no use to examine the stools for the eggs. Even the eggs found at the anal orifice are more or less accidental. In the majority of cases the only way to demonstrate the presence of oxyuris is to find the worm itself. The common mistake of attaching to the demonstration of oxyuris eggs in the stool the same importance as that rightly given to the finding of ascaris eggs is frequently responsible for the failure to diagnose oxyuriasis.

Ankylostomum duodenale (**Strongylus duodenalis, Dochmius duodenalis**) and **Uncinaria Americana.**—If viewed with the naked eye, this worm (Fig. 220) closely resembles oxyuris. It lives, despite its name, almost entirely in the jejunum, and is 6 to 18 mm. long (Heller). The male, much smaller than the female, is provided with a bursa copulatoria (Fig. 220, *a*, *c*). The eggs are oval, 0.05 mm. long, 0.023 mm. broad, and, unlike those of oxyuris, are evacuated in the feces and generally have an indistinct double contour. Ankylostoma, as found in the stool, are usually of a reddish tinge, due to the coloring-matter of the blood sucked from their host. They are hooked so firmly to the intestinal wall that they rarely appear in the stools unless some anthelmintic has been administered. For this reason the

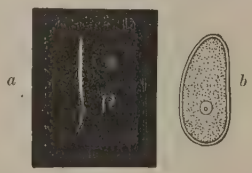


Fig. 219.—Oxyuris vermicularis and egg: *a*, Natural size; *b*, egg (after Heller).

diagnosis must be based upon the history, upon the appearance of severe consecutive anemias (see Examination of the Blood), and principally upon the microscopic demonstration of the eggs in the stools. The last is very easy. Ankylostomum induces a very severe anemia. It occurs in certain vicinities among miners, workmen in tunnels, and brickmakers. In the tropics it is called tropical or Egyptian chlorosis.

To find the worm, the collected stools should be searched for four to six days after the exhibition of an anthelmintic (extractum filicis, thymol). The stools are diluted

with water, decanted carefully, and small fragments are examined upon a black background. The females are found in greater numbers, are larger, and therefore more

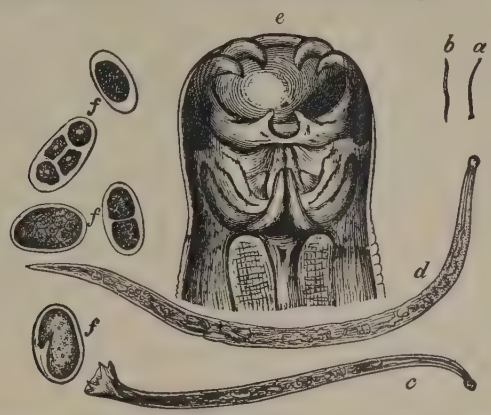


Fig. 220.—Ankylostomum duodenale: *a*, Male (natural size); *b*, female (natural size); *c*, male (enlarged); *d*, female (enlarged); *e*, head (high power); *f*, eggs (after von Jaksch).

easily seen; are colored more intensely red than the males. Leichtenstern found that one could estimate the number of females in the intestines approximately by dividing

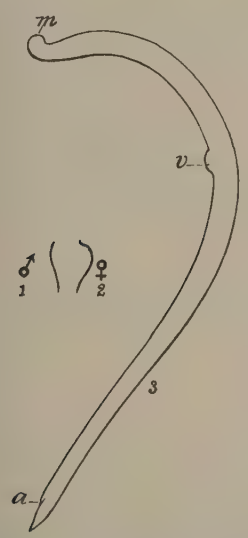


Fig. 221.—New-world hook-worm (Uncinaria Americana) (natural size): 1, Male; 2, female; 3, the same enlarged to show the position of the anus (*a*), the vulva (*v*), and the mouth (*m*) (after Stiles).

Fig. 222.—Four eggs of the New-world hook-worm (Uncinaria Americana), in the one-, two-, and four-cell stages. The egg showing three cells is a lateral view of a four-cell stage. These eggs are found in the feces of patients, and give a positive diagnosis of infection. Greatly enlarged (after Stiles)

the number of eggs found in 1 cc. of a stool of medium consistence by 47. This calculation is of value, since the severity of the disease and the degree of anemia directly

depend upon the number of worms. Eight or more days after the successful cure eggs may be found in the stools, although this does not mean that the cure has failed (Leichtenstern). Infection, according to the old idea, occurred only by swallowing the encapsulated larvæ; but Loos has proved that the larvæ can penetrate the uninjured skin through the hair-follicles, passing from there into the veins, the pulmonary alveoli, the bronchi, larynx, esophagus, stomach, and intestine. The anemia is explained by the loss of blood which the animals produce by their suckers and which is increased by the parasites injecting (like leeches), into the wounds they make, a secretion to prevent coagulation, so that bleeding persists lor a long time. (See Examination of the Blood.)[1]

[Since the publication of Stiles' masterly monograph,[2] the importance of this parasite in the Southern States has been attested by numerous observers. No clinician here should fail to familiarize himself with the general features of the

Fig. 223.—Trichocephalus dispar: Parasite (natural size) and egg (after Küchenmeister).

worm, its eggs, and embryos. The appended diagrams (Figs. 221 and 222) are copied from the above-mentioned source.—Ed.]

Trichocephalus Dispar (Fig. 223).—This is a round-worm, 4 to 5 cm. long, which inhabits the cecum and colon. The eggs are easily recognized and frequently found in the stools. They are somewhat lemon-shaped, colored brownish yellow, and measure 0.05 to 0.02 mm. Ordinarily, it is a perfectly harmless parasite, but if present in very large numbers, it may produce grave, even fatal, enteritis, as has been shown by Leichtenstern and Moosbrugger. The worm is rarely found in the stools, and, like all other intestinal worms, it is very resistant to anthelmintics. (See Examination of the Blood.)

Trichina Spiralis (Fig. 224).—In the first stages of trichinosis the adult or embryo trichina may sometimes, though very rarely, be evacuated in the stools,

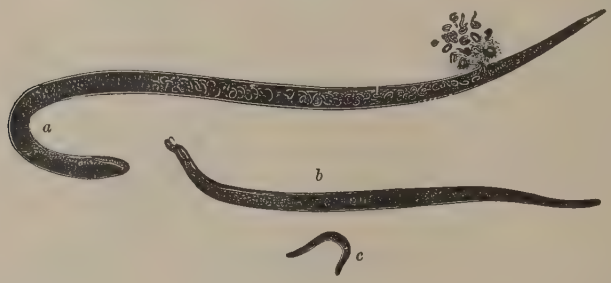


Fig. 224.—Trichina spiralis (greatly enlarged): *a*, Female; *b*, male; *c*, embryo (after Heller).

and so be utilized in establishing the diagnosis. The full-grown male is 1.5 mm. or less in length, and the female 4 mm. or less. (See Examination of Blood, Embryos in Blood, Eosinophiles.)

Echinorhynchus Gigas ("Giant Scratcher").—This worm looks like an ascaris. The males are 7 to 10 cm. long, but the females reach the extraordinary length of 30 to 50 cm. The snout is supplied with numerous hooks with which it bores into the intestinal wall. The hog is its true host, but it has also been found a

[1] Literature: Menche, Zeit. f. klin. Med., 1883; Sahli, Deut. Arch. f. klin. Med., 1883; Leichtenstern, Centralbl. f. klin. Med., 1885, and Deut. med. Woch., 1885; Seifert and Müller, Centralbl. f. klin. Med., 1885.

[2] Hygienic Laboratory Bulletin, No. 10, February, 1903. Report upon the Prevalence and Geographic Distribution of Hook-worm Disease (Uncinariasis or Ankylostomiasis).

few times in the human intestine. Schmidt and Strassburger claim that the embryos enter the grub of the cockchafer (May-bug), and from there pass into the developing insect. The habit, in some regions, of eating raw May-bugs may furnish a possible means of infection.

Anguillula intestinalis and stercoralis (Strongyloides intestinalis) (Fig. 225). —These worms, 0.8 to 2.2 mm. long, are found in the intestinal contents of patients with Cochin-China diarrhea. Leichtenstern found this worm among brickmakers under similar conditions as ankylostomum, sometimes occurring with the latter parasite and sometimes alone. Both Perroncito and the author found it in the workmen employed in the St. Gothard tunnel. We do not know whether it has any pathologic significance. Grassi and Leichtenstern[1] believe that Anguillula intestinalis and stercoralis are only different stages of development (larvæ) of one and the same parasite, which develops in the feces outside of the human body in the sexually ripe stages as Strongyloides intestinalis (formerly called Rhabditis stercoralis). The sporadic occurrence of anguillula infection in Europe has been reported several times recently.[2] (See Examination of Blood.)

Fig. 225.—Anguillula intestinalis and stercoralis: 1, Larva (Anguillula intestinalis); 2, male Anguillula stercoralis; 3, female Anguillula stercoralis (after Perroncito).

Trematodes (Flukes)

Distomum lanceolatum and **hepaticum** are found, although very rarely, in the biliary passages. Their eggs have been found several times in the intestinal contents. They have lids and resemble the eggs of the Distomum pulmonale (Fig. 279) closely, and somewhat the eggs of Bothriocephalus latus. (See Fig. 228, p. 528). They are, however, larger than the latter. Infection occurs by the ingestion of larvæ (called cercaria) in the drinking-water or with raw vegetables. The ova of Distomum lanceolatum measure 0.04 to 0.003; those of Distomum hepaticum, 0.14 to 0.08.

Schistosomia Japonicum.—Tsuchiya has recently reported (Virchow's Arch. 1908, vol. exciii) the occurrence of this trematode in Japan and other parts of eastern Asia as the cause of a new parasitic disease, Schistosomiasis japonica. This worm is related to the distomum and the bilharzia. It inhabits the portal vein and produces serious changes in the liver and spleen with ascites. The eggs are evacuated in the feces. They are characteristically shaped (see the original article).

Besides these trematodes a number of others have recently been found in men, though very rarely, and for the most part in foreign countries: Distomum felineum (sibiricum), D. heterophyes, D. sinense, D. conjunctum, D. crassum, D. Rathonisi, Amphistomum hominis. For their minute description the reader is referred to Schmidt and Strassburger, Die Fäces des Menschen, 2d ed., 1905, Hirschwald, Berlin, and for bibliography to Jaksch-Garrod, Clinical Diagnosis, 1905, London.

Cestodes (Tape-worms)

Almost the only tape-worms of importance, so far as the human body is concerned, are almost exclusively the Tænia solium, Tænia mediocanellata (saginata), and the Bothriocephalus latus. They all inhabit the small intestine. As is well known, tape-worms consist of different generative forms, united to each other, the so-called head, and the sexually adult segments or the proglottides, which develop from and are attached to the head, and in which the eggs develop by hermaphroditism. These segments and free eggs are from time to time evacuated with the patient's stools. The diagnosis of tape-worm infection should never be made from the general symptomatology, but only from the occurrence of proglottides or of eggs in the feces. (See above, p. 521.) The ova are sometimes evacuated with nearly every stool; but too much importance should not be given to their absence in excluding either the existence of a tenia or its persistence after a cure. Despite the presence of the worm,

[1] Ueber Anguillula Intestinalis, Deut. med. Woch., 1898, No. 8.
[2] M. Trappe, Deut. med. Woch., 1907, No. 18, p. 713.

ova are frequently missed in the examination of the stools, especially in the case of tenia. In a case of infection with Tænia mediocanellata observed by the author this failure depended upon the passage of immature segments and the evident arrest of the development of the proglottides. Especially after unsuccessful cures ova are absent from the stools for a long time. The color of the individual proglottides, or of a long, ribbon-like series of them as they appear in the stools, is whitish. Pumpkin seeds, strings of vegetables or animal fiber, or the shreds of mucus in mucous colitis (p. 514), are often mistaken by the laity for tape-worm, mistakes which merely emphasize the importance of the physician observing the suspected material himself.

After the tape-worm has been passed, it is especially important to know whether the head has been secured. (See Figs. 226 to 229 and p. 527 et seq.) If not, the treatment must be considered unsuccessful. If the small end of the tape-worm has been passed without the head being attached, we must search the stools (Boas' stool sieve, see p. 516) carefully for the latter. This is best done by gently mixing the feces with a large quantity of water and straining through a fine sieve, or by allowing the mixture to settle, decanting the upper layers, repeating the process several times, and finally searching for the head at the bottom of the residue. A cathartic should always precede the anthelmintic, to render the search easier. If the head has remained behind, fresh segments or other eggs will be passed within three months. It should be remembered that several tape-worms in the same individual occur not infrequently.

Tænia.—Tænia differ from the bothriocephalus in two points: In the first place, the sexual orifice is situated at the margin of the proglottides,—sometimes

Fig. 226.—Tænia solium: *a*, Head (enlarged); *b*, proglottis (magnified six times); *c*, egg (after Heller).

on one side, sometimes on the other,—looking to the naked eye like a slight excavation in a blunt projection. In the second place, the head has round, sucking discs.

Tænia Solium (Fig. 226).—In its early stages this tape-worm inhabits (as swine measles, Cysticercus cellulosæ) the intermuscular connective tissue of the hog (also the sheep, deer, and dog). Man becomes infected by eating the raw or insufficiently cooked meat of these animals. The worm in man may attain a length of 3 m. and include 900 proglottides. The head is rounded and small, the size of a pinhead (1.3 mm. in diameter), and has a wreath of hooklets in the middle between 4 sucking discs. Continuous with the head is a thread-like, non-segmented portion, about 3 cm. long, to which the string of proglottides is attached; toward the end of the worm the latter are large and broader. Each segment is a little narrower at the upper than at the lower end. Mature segments in a relaxed condition are 9 to 10 mm. long, 4 to 5 mm. broad, and when fresh are somewhat contracted and wavy. Each proglottis contains a uterus with comparatively coarse dendritic branches (Fig. 226, *b*). These details can be seen best with the naked eye by compressing a mature proglottis between two slides. The ova are rounded, almost spherical, about 0.035 mm. in diameter. They have a thick covering with radiating stripes. In eleven to twelve weeks after infection segments are passed. Tænia solium in man may lead to an autoinfection with Cysticercus cellulosæ, the ova reaching the stomach from the patient's dirty fingers or from ripe proglottides regurgitated from the intestines. Infection with tape-worms in contaminated vegetables or drinking-water may also give rise to cysticercus infection.

Tænia Mediocanellata (*Saginata*) (Fig. 227).—The cysticercus stage of this tenia is found in cattle, probably also in goats and sheep. It is comparatively rarely observed in meat, because it occurs in no such great numbers as the Cysticercus cellulosæ of the hog. This fact apparently has some connection with the different modes of life of these animals.

The adult segments of *Tænia mediocanellata*, when relaxed, are 16 to 20 mm. long, 5 to 7 mm. broad. The uterus has fine dichotomous subdivisions, the branches being much more numerous than in Tænia solium. The entire tenia is much larger than Tænia solium (up to 6 m. long) (hence the name saginata—"stuffed"). The head is also much larger, 2.5 mm. broad. It has no hooklets, and was, therefore, formerly called Tænia inermis. The ova do not differ much from those of Tænia solium. (See preceding page in regard to the absence of ova from the stools.) Once in a while single proglottides creep out of the anus. Autoinfection with the cysticercus of Tænia mediocanellata has been observed but once.

Rare Teniæ.—*Tænia cucumerina s. elliptica* (*Diphyllidium cucumerinum*) is 15 to 35 cm. long. The head has four suckers and a protruding snout (rostellum) with numerous rows of hooks. The proglottides have two genital openings, one on each side, at the edge. They are 3 mm. wide, up to 15 mm. long, and are of an elliptic shape. The parasite is most commonly found in the dog, and in man is confined almost exclusively to children. The intermediary host is the dog's flea,

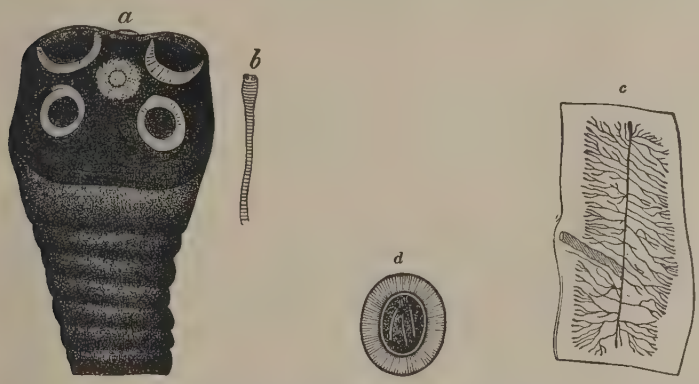


Fig. 227.—Tænia mediocanellata: *a*, Head (enlarged); *b*, head (natural size); *c*, proglottis (magnified six times); *d*, egg (after Heller).

in which the measles (the "cysticercoid") lives. This infects the dog, the latter in turn probably transmitting the disease to children by licking. The ova are 0.03 to 0.036 mm. in diameter.

Tænia nana (*Hymenolepis nana*) is only 10 to 15 mm. long; the segments are 0.5 to 0.9 mm. wide and but one-fourth as long. The head has four suckers and a snout (rostellum) with a single row of hooks. The genital openings are all on the same side of the worm. The proglottides number about 150. The ova are quite transparent and measure 0.03 to 0.037 mm. in diameter. Its developmental history is unknown. The parasite occurs in the intestine in extraordinary numbers (up to 5000), and frequently causes serious digestive disturbances, nervous symptoms, epileptoid states, etc. Most of the observations, particularly the oldest ones, relate to Egypt and Italy, especially Sicily, in which country the parasite appears to be very common. It has also been found in Japan, Russia, England, France, and Germany.[1]

Tænia (*Hymenolepis*) *diminuta s. flavopunctata* is similar to the T. nana. It has been observed in Italy and also in North and South America. The measles live in butterflies and beetles. T. Africana, T. confusa, T. Asiatica, T. (Davainia) Madagascariensis, T. (Hymenolepis s. Dropanidotænia) lanceolata[2] are very rare, at least in Europe.

[1] Mertens, Berlin. klin. Woch., 1902.
[2] Cent. f. Bakt. u. Parasit., vol. xxxi, No. 7.

Bothriocephalus (Dibothriocephalus) Latus (Fig. 228).—This is the largest of all human tape-worms, attaining sometimes the length of 8 m. The mature segments are nearly square (about 5 mm.); the growing segments are three or four times as broad as they are long—10 to 15 mm. by 1 to 4 mm. Its cysticercus (measles, called in this case "plerocercoid") occurs in different fish—pike (*Esox lucius*), eel-pout (*Lota vulgaris*), perch (*Perca fluviatilis*) and in various salmon, especially the trout (*Trutta vulgaris*) as well as in the grayling. The head is flat and oblong, 1 mm. broad, 2 mm. long, with a slit-like sucking groove at the corner on each side. The sexual opening in the proglottides is not at the margin, as in the teniæ, but in the middle of the surface. The uterus is situated around this opening, in the shape of a roset. The eggs have a thin shell, with coarse, granular, mulberry-like contents, and a lid at the top, and can thus be easily distinguished from the tenia eggs. They are, moreover, larger than the latter (0.07 mm. long and 0.045 mm. broad). In the young ova it is not always easy to recognize the lid, as it is either undeveloped or occupies only the extreme pole, so that it is easily overlooked. With bothriocephalus we usually find longer pieces and not individual segments in the stools. The segments do not occur so often as with the teniæ. Hence, searching for the ova is of especial diagnostic importance. As certain cases of pernicious anemia are due to the presence of this parasite, the stools should be carefully examined in every case of severe anemia whose etiology is not plain. The growth in the intestine is very rapid (about 8 cm. a day). The ova appear in the stools twenty-four hours after infection. Although as many as eight worms have been found in

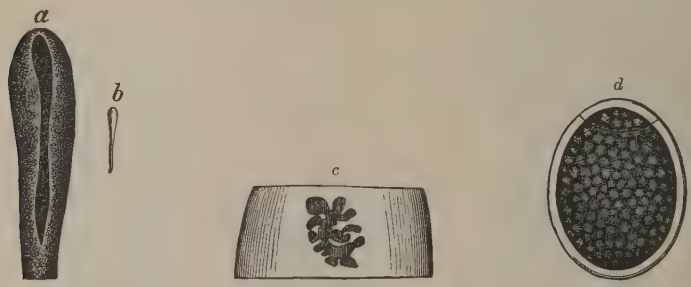


Fig. 228.—Bothriocephalus latus: *a*, Head (enlarged); *b*, head (natural size); *c*, ripe segment (magnified); *d*, egg (after Heller).

one patient, they usually occur singly. The former fact is of importance in estimating the effect of a cure. (For Blood Findings see Examination of the Blood.)

Bothriocephalus cordatus is similar to the Bothriocephalus latus, but is narrower (greatest width, 8 mm.) and not nearly so long. The head is heart-shaped, flattened, and broader than that of B. latus. The ova are similar to those of B. latus, but are a little larger (0.075 to 0.05 mm.). The worm is very rarely found in man (Iceland, Greenland). The usual hosts are the seal, walrus, and dog.

OCCURRENCE OF OTHER ANIMAL PARASITES IN THE FECES

The occurrence of insects in the human bowel or in the feces is rather a curiosity. These cases include the occasional, accidental findings of mites, concerning the significance and specific nature of which nothing is at present known. It seems to be certain that these mites are not identical with the itch-mites. They are probably derived from tainted food (cheese, dried figs, sausage). Somewhat more common, but still quite rare, is the occurrence of the larvæ of flies (diptera) in the human intestine and stools (myiasis intestinalis). Schlesinger and Weichselbaum[1] collected reports of about 100 such cases. Various species are concerned in these cases, especial mention being made of the following: Anthomyia scalaris and canicularis (flower-flies), Sarcophaga carnaria, and Musca vomitoria (carrion flies) and Musca domestica (house-flies). It is assumed that these parasites are introduced with the food in the form of eggs or larvæ. In other cases the larvæ are said to have crawled into the bowel through the anus (especially in infants, Salzmann). They may survive for a long time in the bowel because they do not require much oxygen. Wir-

[1] Wien. klin. Woch., 1902, No. 1 and 2.

sing showed that the sharp hooklets arranged around the individual segments of the larvæ permit their mechanical attachment and forward motion in a direction opposite to peristalsis. There are certain enigmatic cases in which the larvæ of the flies are voided over and over again at considerable intervals, often for years at a time. This indicates either a peculiar constitution of the intestinal canal of the host, which favors the repeated fixation of the ubiquitous parasites after their introduction; or the condition known as pædogenesis, which has been observed in certain diptera, meaning an asexual multiplication of the larvæ. The last-named process has not, however, been noted in precisely the species which here enter into consideration. Concerning the clinical picture, it should be stated that in certain cases the presence of the fly larvæ in the bowel gave rise to no special manifestations; whereas in other cases more or less severe clinical symptoms referable to the digestive organs were probably dependent on the presence of the parasite. In view of the frequently great numbers of the excreted larvæ (up to 1000 individuals), such a pathogenic effect is quite conceivable. Grave symptoms were observed especially by Schlesinger and Weichselbaum (*loc. cit.*). Sometimes the larvæ are vomited. (See p. 431.) See Wirsung for more detailed information and for illustrations and a full bibliographic index.

EXAMINATION OF THE STOOLS WITH REFERENCE TO THE UTILIZATION OF THE FOOD

THE VOLUME OF THE FECES

If the amount of food consumed a day be known, a certain amount of information may be obtained by ascertaining the volume of the feces. This can be done by placing the feces in a measuring cylinder, and adding water until they are completely covered.. If the amount of water added be subtracted from the volume of the water plus the stool, the result gives the volume of the feces.

TEST-MEALS FOR THE EXAMINATION OF THE FECES

By microscopic and chemical examination much may be learned concerning the utilization of food. Strassburger and Schmidt have suggested that the examination be made under more definite conditions than with the ordinary diet. The latest diet suggested by Schmidt has the following composition:

Morning	0.5 liter milk and 50 gm. toast.
Forenoon	0.5 liter porridge, made as follows: 40 gm. oatmeal, 10 gm. butter, 200 cc. milk, 300 cc. water, and one egg.
Midday	125 gm. hashed meat, with 20 gm. butter, fried so that the interior is quite rare; 250 gm. potato, made by cooking 190 gm. potato with 100 cc. milk and 10 gm. butter, the whole boiled down to 250 cc.
Afternoon	Same as morning.
Evening	Same as forenoon.

This diet contains 2234 calories, 102 gm. of protein, 111 gm. of fat, and 191 gm. of carbohydrate. The diet should be given for at least three days, in order to insure that the feces really represent the diet. Under ordinary conditions this occurs after the second day. To be sure of this, 0.5 gm. of carmin in a capsule may be given with the first breakfast. The first stool will then have a reddish tinge.

Against this type of test-meal it may be objected that, as in all test-meals, no account is taken of the individual peculiarities of the patient, and further its constant composition. For a hearty eater, it may be too little. From the standpoint of the health of a subject it is not so important to arrive at conclusions regarding what the patient can eat, as to know how he digests what he ordinarily consumes, so that although one obtains with such a standard diet exact and comparable results, they are not of very great value for diagnostic purposes. For the practitioner the important point is not to compare different individuals regarding their capacity for digestion, but to be able to obtain a diet suitable to correct his digestive disturbance. Hence a diet which does not correspond to the usual dietary habit of the patient gives less useful information on this point. The author is also not altogether certain that harm may not be done by the administration of so full a diet to a patient with a disturbance of digestion.

MICROSCOPIC EXAMINATION OF THE STOOLS TO DETERMINE THE UTILIZATION AND SPLITTING OF FAT

Incomplete utilization of the fats sometimes becomes apparent even in a macroscopic examination of the stool. Stools which contain an abnormal quantity of fat appear light colored, gray, peculiarly glistening. The fat consists partly of a microscopic admixture and partly of larger particles, whose form depends upon the manner in which it was administered. Under the microscope the fat is seen to consist of fat-drops and of needle-like crystals. (See Fat-crystals of the Sputum, Fig. 278, *a*, p. 707.) Their appearance depends upon the melting-point of the respective fats, and upon whether the fats are found in the stool unchanged, split up, or saponified. Neutral unsaponified fats may appear either as drops or as needles. Soaps usually appear as thick, short needles or flakes; free fatty acids, as needles. The addition of osmic acid colors fat microchemically brown to black. Yet this reaction is only characteristic for fats which contain oleic acid; whereas other fats either remain unstained or require the addition of alcohol to bring out a color. The addition of an alcoholic solution of Sudan red colors all neutral fats. Fatty acids differ from neutral fats in their ready solubility in weak solutions of sodic hydrate. Fatty soaps, in contrast to fatty acids and neutral fats, do not dissolve in ether.

Normal stools contain a moderate number of *fat-needles*, which represent the fats that are not easily melted, and are, therefore, less readily absorbed. Fat-drops are not so common except after abundant ingestion of milk or easily melted fats. They usually signify an insufficient utilization of the fats, as does also an abnormal abundance of fat-needles.

The stools may be abnormally fatty in disease of the pancreas, and in cases when the bile is shut off from the intestine (steatorrhea). But in both cases emulsified fat, such as is contained in milk, seems to be well absorbed. (See Chemical Examination of Feces, p. 541.)

MICROSCOPIC EXAMINATION OF THE STOOLS TO DETERMINE THE UTILIZATION OF STARCH

The microscopic appearance of starch is well known (p. 428, Fig. 201, *i–n*). Starch-granules are characterized microchemically by their blue or violet color after the addition of Lugol's solution. Well-preserved starch-granules are rarely found in the normal feces of an adult, but they may occur in the stools of infants improperly fed with starches. Statements in regard to the absence of starch-granules in healthy adults are of limited value, because after an abundant ingestion of starches part of the starch-granules are evacuated undigested. It should also be noted that under normal conditions starch-granules which are inclosed in plant cells escape digestion; so, too, does raw starch.

An abundance of starch-granules in the stools of adults is pathologic, and is usually a sequence of diarrhea or of gastric hyperacidity. The absence of pancreatic juice does not seem to cause the appearance of pathologic quantities of starch in the feces, because the starches, along with the other carbohydrates, are utilized very extensively by the intestinal bacteria under formation of acids. Deficiency of bile in the intestinal contents is not responsible for any increase of starch in the stool, as the bile contains only traces of a diastatic enzyme, which are of no practical importance.

MORPHOLOGIC EXAMINATION OF THE FECES TO DETERMINE THE UTILIZATION OF THE MUSCLE-FIBERS OF THE CONNECTIVE TISSUE AND OF THE OTHER PROTEIDS OF THE FOODS. (See also Chemical Examination of the Feces.)

Muscle-fibers and Connective Tissue.—Meat-fibers in the stools are easily recognized microscopically by the more or less well-preserved transverse striation (Fig. 229, *aa*). The more thorough the digestion, the less distinctly this appears, and the more are the ends of the fragments rounded off. The fibers are tinted brown in part by their own color and in part by the color of the feces. Microchemically, they are characterized by the appearance of a red color upon heating with Millon's reagent.[1] Undigested muscle-fibers are constantly found in the feces of a person upon a mixed diet. The amount becomes pathologically increased in diarrhea, in fever, and in other disturbances of the digestive chemism. According to Schmidt, the presence

[1] Millon's reagent is a dilute filtered solution of mercury in fuming nitric acid, see p. 604, Note 1, for its preparation.

of nuclei of muscle fragments occurring in feces indicates a complete absence of the pancreatic function. On the other hand, their disappearance does not of itself justify the conclusion that the function of the pancreas is perfect (decomposition). (See Schmidt's nuclei test, p. 508.)

Large fragments of connective tissue are generally readily recognized even macroscopically by their fibrous structure; this also characterizes them microscopically, as does their pronounced clarification upon the addition of acetic acid. They can be distinguished from mucous shreds by their much firmer consistence, more distinctly fibrous structure, and the disappearance of the latter structure after the addition of acetic acid, which renders mucus striated. They differ from fibrin in the absence of the reticular or trellis-like appearance. With an ordinary diet such connective-tissue remains occur frequently in the stools in health. To discover connective tissue, the stools should be stirred with water and examined over some dark substance (black plate). (See Examination of Sputum.) The connective-tissue fragments may then be recognized as white fibers.

According to Kühne's[1] and A. Schmidt's investigations, raw connective tissue is digested by the gastric juice only, whereas cooked connective tissue is also easily dissolved by the pancreatic juice. Hence the amount of connective-tissue remains in the stools depends upon the amount ingested, upon the degree of boiling or roasting the meat, and upon the gastric function. Starting from the same premises that the author made use of in devising his desmoid test, Schmidt estimates the gastric

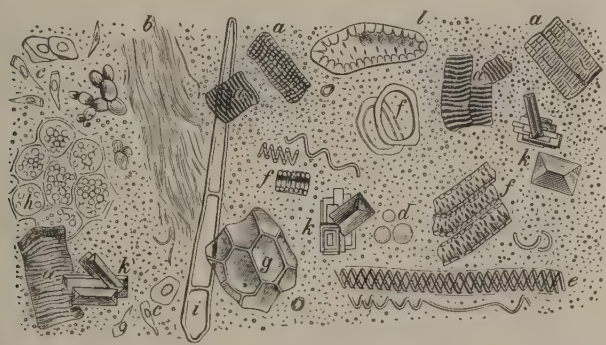


Fig. 229.—Microscopic elements of normal feces: *a*, Muscle-fibers; *b*, connective tissue; *c*, epithelial cells; *d*, white blood-corpuscles; *e*, spiral vessels of plants; *f–h*, vegetable cells; *i*, plant hairs; *k*, triple phosphate crystals; *l*, stone-cells. Scattered among these elements are micro-organisms and débris (after von Jaksch).

digestion by determining the amount of connective tissue in the stools after the ingestion of his test diet (p. 529), since experience has convinced him that the stools do not normally contain any connective-tissue remains after the ingestion of 125 gm. of slightly roasted chopped meat. He claims[2] that the macroscopic appearance of muscle-fibers in the stools of a patient who has ingested a test-meal of 125 gm. of very slightly roasted chopped meat demonstrates some severe damage to the intestinal digestion. On the other hand, the occurrence of macroscopically visible fragments of connective tissue is indicative of insufficient gastric digestion, because connective tissue, unless it is cooked to pieces, is dissolved only by peptic digestion.

Coagulated egg-albumen and casein may be found in amorphous masses in normal stools, and more especially in stools denoting insufficiently utilized food. The coarse, granular lumps of casein are important diagnostically, because they compose the major part of a poorly digested infants' stool. A normal infant's stool should be homogeneous and even. The curds of casein are, for the most part, colored a brownish to yellow externally by the fecal coloring-matter or by altered bile-pigment. Inside they often remain white. Microchemically, they are characterized by an almost complete solubility in 5 per cent. HCl and KOH solution. From the latter solution they can be precipitated by acetic acid and redissolved in an excess of the same. The well-known microscopic "yellow granules," which

[1] Verhandlungen des naturforschenden Vereines, Heidelberg, N. F., 1, 1877.
[2] Deut. med. Woch., 1899, No. 49, p. 811.

are almost visible macroscopically, which frequently occur in pathologic stools, have been named by Nothnagel "mucous granules." They are characteristic yellowish flakes without a definite structure. According to Schmidt and Strassburger, they are not mucus, but probably in part remnants of muscle, in part casein or proteid remains.

INDIGESTIBLE FOOD RESIDUE

In every normal stool the constituents of the food which are indigestible reappear. All cellulose-like substances are not attacked by the digestive ferments, and only very incompletely by the bacteria of the intestine (plant hairs and spiral vessels, vegetable cell framework, etc.) (Fig. 229, *e*, *i*, *l*). Various constituents of animal food also remain undigested; for instance, large connective-tissue fragments, pieces of cartilage, and elastic tissue (Fig. 229). According to Strassburger and Schmidt, the stools after the ingestion of chicken or other fowl contain minute bits of skin and remnants of feathers, which can be recognized as such; and after the ingestion of fish, scales and bones.

Fig. 230.—Apparatus for testing fermentation in the stools.

FERMENTATION OF THE FECES AFTER EVACUATION

Ad. Schmidt and his school have recently endeavored to draw conclusions in relation to intestinal function from the manner in which the feces ferment after evacuation, *i. e.*, from the gases which are thus formed. Such fermentation, if it be very marked, depends essentially upon an abnormal content of carbohydrates in the stools.

Schmidt's directions for performing his fermentation test are as follows: "5 gm. feces are selected from a well-mixed stool by means of a wooden spatula. Much less is taken from a hard than from a watery stool, in order that one may work with approximately equal amounts of dry substance. No greater accuracy is essential for diagnostic purposes. The material is well stirred with water, put into the bottom glass (*a*) of the fermentation apparatus (Fig. 230), which is corked with a rubber stopper, taking care to prevent the entrance of air-bubbles. Tube (*b*) is filled with tap water and closed with a small rubber stopper, the same precautions against admission of air-bubbles being taken. The apparatus is then assembled as in the figure and left in an incubator at 37° C. for twenty-four hours. Tube (*c*) has a tiny hole at the top and should contain no water. If gas develop from the feces, the corresponding amount of water will be driven into tube (*c*) and its height can be read off."

Schmidt considers the test positive (*i. e.*, indicating an insufficient utilization of the carbohydrates) when about 1 gm. of dry fecal substance passed after a test diet (p. 529) produces more than one-quarter tube of gas.

The author, having had no experience with the test, refers to the original article.[1]

BACTERIA OF THE FECES

Feces consist to a large extent of the body substance of micro-organisms. Before Koch's plate-culture methods became known, it seemed to be quite impossible to isolate the bacterial admixture of a normal or pathologic stool. But since then, by the isolation of individual varieties, some light has been thrown on this subject. Bienstock was the first to study the question exactly. He decided that only four kinds of bacilli were to be found in the intestine, one of which was the specific decomposer of the proteids; and that there were no micrococci, because, being non-spore-bearing, they were destroyed upon entering the digestive tract by the hydro-

[1] See particularly A. Schmidt, Deut. Arch. f. klin. Med., vol. lxi, and A. Schmidt and J. Strassburger, Die Fäces des Menschen, Berlin, second edition, 1905, A. Hirschwald.

chloric acid of the stomach. Later investigators, who worked with anaërobic culture methods and varied culture-media, could not corroborate these results; they showed that the number of varieties was much larger.

The possibility of making use of bacteriologic examinations of the intestinal contents except for the demonstration of specific pathogenic bacteria for practical clinical purposes seems, therefore, less hopeful than Bienstock's investigations suggested. An essential difficulty of an exact study of the intestinal flora depends upon the fact that many of the normal bacteria and of those occurring under pathologic conditions in the stools are destroyed through the physiologic action of the organism, or are so specifically adapted to the vegetative conditions in the intestines that they cannot be cultivated in vitro. There is always a striking contrast between the enormous number of bacteria which the microscope shows and the relatively few colonies which one can cultivate. This is a great obstacle to progress in our knowledge, and especially so because intestinal bacteriology plays a very important rôle not only in intestinal diseases, but also in the etiology of other infectious maladies.

The Bacterial Species Which Occur in Normal Feces

The bacterial and fungus species of normal intestinal contents have been more fully studied of late. (See the comprehensive treatises of Mannaberg,[1] Schmidt and Strassburger.[2] These studies have proved that by far the majority of fecal bacteria belong to the colon group. Among the better known species are the Bacillus lactis aërogenes, the Bacillus subtilis, Bacillus proteus vulgaris, Bacillus butyricus (Bacillus amylobacter). It is worthy of note that bacteria known to be pathogenic, such as staphylococci, streptococci, and pneumococci, are frequently, perhaps constantly, present in normal feces, but they are of no diagnostic significance unless in sufficient numbers to be noticeable in dried smears. A rapid estimate of the bacterial flora in the feces may be obtained by studying a particle of the stool (mixed with water, if necessary) under the microscope (using the oil-immersion lens and a partially closed diaphragm). The numbers, shape, and motility of the bacteria should be studied. For more exact microscopic examination, dried specimens are prepared in the same way as from the sputum (see pp. 709 and 715), and stained either with carbolfuchsin or by Gram's method (p. 715). To distinguish a group of bacteria which takes different stains it is better to stain first with Gram and then with a dilute solution of carbolfuchsin (1:10). The usual culture-media (bouillon, peptone gelatin, and agar plates) may be employed to determine the species. Faintly acid beer-wort in agar plates has been recommended for cultivating the intestinal bacteria. Several species which do not grow in the ordinary nutrient media thrive upon this. Anaerobic cultures are occasionally necessary for fecal bacteria.

The investigations of Escherich, Moro, and Tissier on the intestinal bacteria of infants are interesting. Escherich found the meconium of the new-born free from bacteria. The first bacteria are found four to seven hours after birth at the earliest. According to Strassburger and Schmidt, most of the bacteria in the stools of breast-fed children are Gram-positive. According to the investigations of Moro[3] and Tissier,[4] there are probably two chief species. The one, aërobic, is designated by Moro as Bacillus acidophilus, the other, anaërobic, by Tissier, as Bacillus bifidus. Both species require special cultivation: the former in an acid, the latter in an air-free medium. The same investigator found the bacterial flora in the stools of infants fed with cow's milk less characteristic and more diversified. The Gram-positive bacteria do not preponderate to the same degree. Hence the stools of infants fed upon cow's milk constitute a transition between those of nursing infants and those of adults, in which the Gram-positive bacilli normally play quite a subordinate part, so that very frequently almost no Gram-positive bacteria are found in the normal adult stool. Under physiologic conditions only colon bacilli and a few colonies of Bacillus lactis aërogenes can be cultivated from the stools of adults.

The examination of the stools, of course, furnishes information concerning the bacteria of the lowest portion of the gut only. The contents of the small intestine, as occasionally obtained from fistulæ, are entirely different. They are not only much poorer in bacteria, but also contain different species, especially the liquefying bacteria, Bacillus coli commune, Bacillus lactis aerogenes, staphylococci, and other species are likewise met with here as well as in the large bowel.

[1] See the introduction to Nothnagel's Diseases of the Intestines and Peritoneum, in which there is also a complete bibliography.

[2] Die Fäces des Menschen, etc., second edition, 1905, A. Hirschwald, Berlin.

[3] Jahrb. f. Kinderheilk., 1900, vol. lii.

[4] Recherches sur la flore intestinale du nourrison, G. Carré et C. Nord, Paris, 1900.

The Quantity of Bacteria in the Feces

According to the above statements, cultures furnish no information as to the quantity of bacteria in the feces, because only a small fraction of all fecal bacteria can be cultivated artificially (according to Strassburger,[1] barely 1 per cent.). The others are, however, not necessarily dead, as Strassburger assumes, but perhaps they are merely so especially adapted to the vegetative conditions of the bowel that they do not thrive elsewhere. According to Strassburger, bacteria comprise about one-third of the dry residue of the feces. He estimates that in twenty-four hours a healthy adult evacuates about 8 gm. of bacteria (weighed dry); in diarrhea there is an increase up to 14 to 20 gm.; in constipation, a decrease to 5.5 gm. For in diarrhea the bacteria obtain more nutriment, while in constipation the pabulum is diminished on account of the more complete assimilation of the food. Reduction of the food lessens the daily quantity of bacteria (according to Strassburger). He was unable to demonstrate an influence of the intestinal antiseptics upon the daily quantity of bacteria, but this, of course, does not prove that intestinal antiseptics are entirely useless.

The quantitative determination of the bacterial content of the feces is, as suggested above, very difficult, because the ordinary procedures for counting bacteria by means of plate cultures are inapplicable, since very few fecal bacteria will grow in cultures. On the other hand, the purely morphologic counting methods based upon the method of counting the blood-corpuscles (direct counting in dilutions) are unreliable, on account of the difficulty of obtaining uniform suspensions. Strassburger, therefore, attempts to estimate their weight. He first isolates the bacteria, freeing them from the coarser constituents of the feces by centrifuging watery infusions, and then mixing with double the quantity of alcohol. The bacteria can then be centrifuged, dried, and weighed. From the quantity of bacteria found in a cubic unit of stool Strassburger then calculates the daily quantity. In this procedure all particles of stool which are of the same size are calculated as bacteria.

PATHOGENIC BACTERIA OF THE FECES WHICH ARE IMPORTANT FROM A DIAGNOSTIC STANDPOINT

Tubercle Bacilli (Fig. 280).—In intestinal tuberculosis these bacilli are found in the feces, and are, therefore, of diagnostic importance. The stools may, however, contain them, even though there is no intestinal tuberculosis (if the phthisical patients swallow their sputum). Searching the stools has even been recommended for the diagnosis of lung tuberculosis in cases of irresponsible persons who swallow the sputum. The usual dry preparation properly stained is sufficient. (See p. 709.) Although in the examination of sputum previous treatment with dilute sodium hydroxid or digestive enzymes is often successful, it is rarely of use in the examination of feces (see p. 714), because the latter consist chiefly of indigestible substances, which are insoluble in sodium hydroxid. But it may be serviceable in the examination of mucopurulent particles which have been isolated from the mass of feces. We do not know whether, under certain conditions, putrefaction may destroy tubercle bacilli in the intestine. At any rate, we cannot always demonstrate tubercle bacilli in the stools even when there is undoubted intestinal tuberculosis. Perhaps this is on account of the dilution of the content of tubercle bacilli by the abundant particles of food. Tubercle bacilli are most readily found in the purulent or bloody particles of diarrheal stools. Generally speaking, direct searching through solid stools is less promising. Nevertheless, they may quite frequently be demonstrated in solid stools, if, as Hamburger recommends, we mix a piece of feces the size of a pea with a few centimeters of water, then centrifuge gently to remove the coarser pieces, dilute the supernatant cloudy fluid with a double volume of alcohol, centrifuge once more, and then examine dry preparations of the remaining precipitate, which consists almost exclusively of bacteria. As tubercle bacilli in the feces may be due to swallowed sputum, we can diagnose intestinal tuberculosis only if bacilli be found in the feces, during attacks of diarrhea, together with pus and blood in the stool, and the other corresponding clinical symptoms. The tubercle bacillus must be carefully distinguished from the smegma bacillus, which is said to occur at the anal orifice and might have become mixed with the feces. (See p. 693.) This is of importance when the bacilli are found in a particle from the surface of a solid stool. Other acid-fast bacilli must be considered in the differential diagnosis (p. 713 et seq.). Rosenberger regularly finds tubercle bacilli in the stools in miliary tuberculosis. [Bruns[2]

[1] Zeit. f. klin. Med., vol. xlvi, parts 5 and 6.
[2] Jour. Amer. Med. Assoc., September 18, 1909, liii, p. 909.

showed that laboratory distilled water, when permitted to stand for some time, became the habitat of an acid-fast bacillus, easily mistaken for the tubercle bacillus. This paper and the almost universal failure of careful workers to confirm Rosenberger's findings of tubercle bacilli in the blood also discredit his observations upon stools.—Ed.]

Bacilli of Cholera, better, Cholera Vibrios (Comma Bacillus) (Fig. 231).—The demonstration of cholera bacilli is of great importance in the early diagnosis of the first cases of a cholera epidemic; and also in detecting the so-called "cholera bacillus carriers," *i. e.*, individuals who, during cholera epidemics and in the neighborhood of cholera patients, harbor the cholera vibrios in their intestines, and so are capable of transmitting the disease without being sick themselves. This is of great prophylactic importance, and also essential in determining when further isolation of cholera convalescents can be dispensed with. The bacilli are constantly present in the stools of cholera patients, and at times in very great quantities. By demonstrating their presence, the differential diagnosis between cholera nostras and Asiatica, formerly so very difficult, may be made with certainty in an isolated case and without first waiting for an epidemic. A dry specimen should be prepared from one of the little mucous flakes suspended in the stool, and then stained in the ordinary way with fuchsin, gentian-violet, or methylene-blue. (See Examination of Sputum.) Cholera vibrios (Fig. 231) are slightly bent rods with an average length of 1.5 and width of 0.4 μ. They are bent not only in one plane, but so as to resemble the thread of a screw, and are so arranged as to form varying shapes, *e. g.*, the letter S. Actively

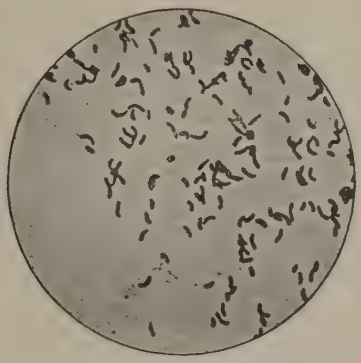


Fig. 231.—Cholera bacilli (× 1000) (after Weichselbaum).

motile, they possess a single terminal flagellum, which can be stained with the ordinary method for staining flagella. The vibrios themselves are Gram-negative.

A microscopic examination for comma bacilli is not enough to make a diagnosis absolutely sure, because there are other comma-shaped bacilli, as, for example, those of Finkler and Prior, found in cholera nostras. Moreover, a negative microscopic result without any culture tests would not permit the absolute exclusion of cholera. The vibrios grow best upon rather strongly alkaline media. Kolle obtains the best results by adding 3 cc. of a 10 per cent. sodic hydrate solution to 100 cc. of a medium neutral to litmus. The usual plate cultures with gelatin made alkaline as above are employed for demonstrating the organisms culturally. After twenty-four to thirty-six hours numerous liquefying colonies will be found, from which gelatin streak and potato cultures are to be made. The gelatin stab cultures are characterized by the fact that the gelatin on the surface is liquefied very rapidly in a funnel-shaped depression, whereas in the interior the liquefaction occurs only as a slender canal along the line of inoculation. On potato the comma bacilli grow rather slowly at 20° C., as a thin, gray-green coating. The use of agar plates is very important for a rapid diagnosis of cholera, because they can be kept at incubator temperature. The agar must be strongly alkaline. Petri dishes make the best plates. Before inoculation the covers should be removed and the plates turned upside down and dried for about five minutes in a drying chamber at 60° C. A very small amount of the suspected material is, as slowly and evenly as possible, rubbed upon the surface of the plate with a Drigalski spatula (a glass rod bent at a right angle).

According to Kolle, isolated colonies which can be identified are obtained after eighteen hours at 36° C. (see below).

The comma bacilli may sometimes be found in the vomitus.

Comprehensive data relative to the bacteriologic demonstration of cholera bacilli are to be found in Pfeiffer's extensive article in Deutsche medicinische Wochenschrift, 1892, No. 36.

A government publication by Koch, Kirchner, and Kolle (November 6, 1902) describes the bacteriologic methods of diagnosing cholera and contains the necessary information for studying the suspected material.

If the comma bacilli be cultivated in a sterilized solution of 1 gm. of peptone and 0.5 gm. of NaCl to 100 cc. of water, an especially favorable medium, and concentrated sulphuric acid be then allowed to flow underneath, a red discoloration will occur at the line of junction of the two fluids, due to the indol and nitrites contained in the culture (nitrosoindol). This pigment used to be called cholera-red, but the name is not quite correct, because the same indol reaction occurs also with other bacteria. If the culture be not a pure one, the nitrosoindol reaction is of no diagnostic importance. Cholera vibrios may be excluded if the reaction does not occur, provided that true cholera bacilli sown upon the same medium do furnish the color. The peculiar motility of the cholera vibrios is especially marked in the aqueous peptone cultures.

Biologic methods (*Pfeiffer's test* and *agglutination*) are best for exact identification of pure cholera cultures transferred from the surface and the water of condensation of agar slants and isolated best by means of agar plates. These examinations are necessary especially at the beginning of an epidemic, because of the occurrence of other vibrios resembling those of cholera, which may lead to confusion.

Pfeiffer's (bacteriolytic) test is accomplished by injecting into the peritoneal cavity of young guinea-pigs a lethal amount of the bacilli in question simultaneously with an injection of a definite amount of the serum of animals immune to cholera. If they be true cholera bacilli, they will be dissolved within in short time in the peritoneal cavity. Pfeiffer [1] claims that other bacteria, no matter how much they may resemble cholera bacilli, do not show this purely specific reaction.

The Agglutination Test for Cholera.—If serum from animals immunized against cholera be added to a liquid culture of cholera bacilli, the latter lose their motility and agglutinate in clumps, very much as do typhoid bacilli when acted on by typhoid serum. (See Widal's Serum Diagnosis, p. 857, et seq.[2]) The importance of these different methods of examination in the demonstration of cases of cholera depends upon circumstances. The morphologic and cultural tests are sufficient for the recognition of suspicious cases during an epidemic. The demonstration of countless vibrio colonies in agar cultures made directly from the feces is especially important. On the other hand, great caution is necessary in the exclusive employment of the culture method with peptone water (see above), because other vibrios may be obtained in great numbers, and this is not the case with the agar plates unless cholera exists. The use of the biologic tests with pure cultures is more certain in all cases, and they must certainly be employed to detect the first case in an epidemic in places where cholera has not previously existed.

Typhoid Bacilli.—Typhoid bacilli have been demonstrated in the stools of typhoid patients from the second or third week on. Culture methods (isolation and plate cultures) are, of course, necessary for each demonstration, since the typhoid bacilli do not possess any typical morphologic peculiarities. This demonstration is, however, so complicated and takes so long that it is of much less practical importance in the diagnosis of typhoid fever than in the discovery, so important to prevent the occurrence of epidemics, of "typhoid carriers." The latter are individuals who, after their fever, or even without being manifestly sick, harbor typhoid bacilli and so endanger others. The reader is referred to text-books on bacteriology, and especially to Pfaundler's work [3] on the differentiation of typhoid and colon bacilli; and to Kühne's work upon the early diagnosis of typhoid (Jena, 1904). A brief account of some of the most important methods of demonstration is given here.

Most methods consist in the preparation, from the stools, of plate cultures to the

[1] Zeit. f. Hyg., 1895, vol xix, p. 75.

[2] Kolle and Wassermann, Handbuch der pathogenen Mikroorganismen, 1904; Kolle and Hetsch, Lehrbuch der experimentellen Bakteriologie, 1909; W. Kolle and G. Gotschlich, Zeit. f. Hygiene und Infektionskrankh., 1903, vol. xliv, part 1, p. 1.

[3] Kolle and Wassermann, Handbuch der pathogenen Mikroorganismen, 1904, vol. i.

media of which are added certain substances which are known to have a different influence upon the growth of typhoid and other fecal bacteria, especially the colon bacillus. In this way a degree of selection is favored, or at least there is produced a distinctive macroscopic appearance to the individual colonies sufficient to allow of their recognition and to point the way to other more accurate methods of examination.

The author selects for description the method of Drigalski and Conradi.[1] The so-called Drigalski's agar is prepared as follows:[2]

(*a*) About 3 pounds of chopped beef are left to stand in 2 quarts of water for twelve to twenty-four hours. The meat is then pressed and the fluid obtained is boiled and filtered. 20 gm. of Witte's peptone, 20 gm. nutrose, and 10 gm. salt are added, after which it is boiled again, filtered, and 60 gm. of agar added. This mixture is then boiled in streaming steam for three hours and made faintly alkaline to litmus, filtered, and boiled again.

(*b*) Litmus lactose solution. The litmus solution, prepared according to Kubel-Tiemann, may be obtained from C. A. F. Kahlbaum in Berlin. Ten cc. litmus solution is boiled for ten minutes, 30 gm. chemically pure milk-sugar added and the mixture boiled for fifteen minutes.

(*c*) *a* and *b* are mixed while still hot, well shaken, and the mixture made alkaline again by the addition of 4 cc. of a sterile 10 per cent. solution of anhydrous soda. Finally, 20 cc. of a solution of 0.1 crystal violet (Mark O, Höchster-Farbwerke) in 100 cc. of sterile water is added. This should be freshly prepared each time. The mixture is poured into 200 cc. flasks and can be kept for a long time.

Plate cultures can be prepared from this medium by selecting a small amount of the feces to be examined and rubbing it over the surface of the hardened agar by means of a Drigalski spatula. Four plates can be inoculated from one streaking of the spatula, and so successive dilutions obtained for isolation of the germs. Instead of Petri dishes, larger covered dishes, 15 to 20 cm. in diameter, and 1 to 2 cm. deep, are recommended. The agar is poured into the plates to a depth of not less than 2 mm. Before inoculation the surface of the medium must be freed from water of condensation by setting the uncovered plates upside down in the drying oven. For cultivation, the plates are kept at 37° C. with the cover down, so as to avoid any water of condensation. Upon this medium there is a blue area about the typhoid colonies, while the colon bacilli, on account of the production of acid, are surrounded by a red zone. The existence of colonies which do not alter the blue color of the medium is not, of course, sufficient for the demonstration of typhoid bacilli, but merely points to their selection for more careful investigation by the methods to be described below, and excludes the greater proportion of the colonies of the colon group.

Another culture-medium which is recommended for a bacteriologic diagnosis of typhoid is E. Roth's[3] and Ficker and Hofmann's[4] caffein bouillon. This favors the growth of the typhoid and inhibits that of the colon bacillus. It is prepared as follows:[5]

Sufficient soda solution is added to stock bouillon to neutralize the latter, using tested phenolphthalein as an indicator. The bouillon is then sterilized and 80 to 100 per cent. of its volume of a 1 per cent. caffein solution is added. In preparing the latter, pure commercial caffein is dissolved in boiling distilled water. The bouillon is inoculated with a tiny amount of the feces to be examined, and kept at 37° C. This exalts the typhoid bacilli, and the exalted bouillon culture is then prepared and examined on plates according to Drigalski's and Conradi's methods.

For isolating typhoid bacilli from the stools Loeffler's selective malachite green has been much employed recently. Loeffler's later modifications of the method are to be found in the Deutsche medicinische Wochenschrift, 1908, No. 39, p. 158.

If some of the colonies obtained according to one of the above methods suggest those of the typhoid bacillus, an orientation agglutination test is made. A platinum needle is inoculated with a tiny particle selected from one of the suggestive colonies, and mixed upon a glass slide with a drop of typhoid immune serum of a titre homologous strain. The mixture is then covered with a cover-glass one edge

[1] Zeit. f. Hygiene und Infectionskrankh., 1902, vol. xxxix.

[2] According to Heim, Lehrbuch der Bakteriologie, third edition, Stuttgart, 1906.

[3] E. Roth, Hyg. Rundschau, 1903, pp. 489 et seq.; Arch. f. Hyg., 1904, vol. xlix, p. 199 et seq.

[4] Ficker and Hofmann, Hyg. Rundschau, 1904, p. 1 et seq.; Arch. f. Hyg., vol. xlix, p. 229 et seq.

[5] Günther, Bacteriologie, Leipzig, 1906, G. Thieme.

of which rests upon a second cover-slip, so that a wedge-shaped sort of chamber is formed. If the organism be typhoid bacillus, agglutination will occur after about twenty minutes. An exact quantitative agglutination test (see Widal reaction) is more accurate, especially if confirmed morphologically and culturally (see below).

Morphologic Characteristics.—The typhoid bacillus is a plump rod, 1 to 2 μ long, negative to Gram (see p. 715 et seq.), and cannot be distinguished from the colon bacillus. It is actively motile in fresh cultures, especially plainly in the water of condensation from agar cultures, and in bouillon cultures, in contrast to most colon bacilli, which are non-motile, or, at best, inactive. The flagella stain brings out many peritrichous cilia, which are much more numerous and better developed than those of the colon bacillus.

Cultural Characteristics.—The typhoid bacillus grows as well at room as at incubator temperature. Gelatin is not liquefied by the typhoid any more than by the colon bacillus. The former sometimes grows upon gelatin in the form of long threads. The following refers to its growth at incubator temperature:

It grows slowly upon milk without causing coagulation, while the colon bacillus usually curdles milk in twenty-four to twenty-eight hours. Like the colon, the typhoid bacillus grows upon bouillon without forming a scum, but, unlike the former, it does not produce indol. Kolle tests for indol in this way: 1 cc. 0.02 per cent. potassium or sodium nitrite solution is shaken up with 10 cc. of the culture, and a few drops of pure sulphuric acid are added. Indol turns the fluid red (nitroso-indol).

Unlike most bacilli of the colon group, the typhoid grows upon 2 per cent. glucose without the production of gas. Another characteristic difference between the two germs is their growth upon media colored with litmus. Petruschki's litmus-whey is most convenient. It is rather difficult to prepare, but can be obtained from C. A. F. Kahlbaum in Berlin. Most colon bacilli change this medium to an intense red, while typhoid bacilli either do not change it at all or at most tinge it very faintly. Certain alkali-producing bacteria occurring in the stools color the litmus-whey an intense blue, and so would not cause confusion. The tint can be distinguished best after twenty-four hours' growth, and controlled by tubes inoculated with proved typhoid organisms and by tubes not inoculated. For proper comparison, care must be taken to inoculate the tubes with the same amount of material.

The growth upon potato is, to a certain extent, characteristic. The colon bacillus forms a grayish-brown coating, whereas the typhoid frequently forms a colorless, quite invisible film, which can only be demonstrated by lifting it up with a needle. Numerous variations do, however, occur, depending upon the reaction of the potato. The invisible growths occur only upon potato, which usually exhibits a slightly acid reaction.

Its growth upon neutral red agar is of value. Rothberger first employed this medium. Scheffler[1] modified it as follows: 1 cc. of a concentrated sterile aqueous solution of neutral red is added to 100 cc. of the ordinary 0.3 per cent. glucose agar. The color should be a dark red; otherwise the reaction must be corrected. A stab culture of typhoid bacilli after twenty-four hours at 37° C. shows no change in the color, whereas colon bacilli produce a yellow discoloration with a green fluorescence in the area about the stab. The alkali-producing intestinal bacteria and the dysentery bacilli behave upon neutral red agar like the typhoid bacilli.

Loeffler employs media containing malachite green, not only for isolation, but also for more exact differentiation. (See his work, p. 537.) Elsner[2] has announced a method of isolating typhoid bacilli more easily from the stools, and also differentiating them from colon bacilli. He employs a faintly acid culture-medium containing potassium iodid. Piorkowski[3] has attempted to achieve the same result by the employment of plate cultures upon a medium to which alkaline urine has been added.

To overcome the difficulties of a bacteriologic diagnosis of typhoid bacilli in contradistinction to certain varieties of colon bacilli, Pfeiffer[4] tried to characterize the typhoid bacilli by some biologic reaction with the serum of animals immune to typhoid. This reaction as described by Pfeiffer is performed upon animals in exactly the same way as the cholera reaction (see above). It may now be replaced

[1] Centralbl. f. Bakt., 1900, i, vol. xxviii, p. 203.

[2] Zeit. f. Hyg. u. Infectionskrankh., 1895, vol. xxi; and Brieger, Deut. med. Woch., 1895, No. 50, p. 835.

[3] Berlin. klin. Woch., 1889, No. 7, p. 149.

[4] R. Pfeiffer and W. Kolle, Ueoer die specifische Immunitätsreaction der Typhusbacillen, Zeit. f. Hyg., 1896, vol. xxi, part 2.

by the convenient Gruber-Widal agglutination reaction of typhoid. (See later, Blood-examination, p. 857.) To be sure, the utility of this procedure for recognizing typhoid bacilli has of late been questioned, although the value of the serum reaction as a diagnostic measure is now hardly ever disputed.

Dysentery Bacillus.—While tropic dysentery seems to be an amebic disease (see p. 519), F. Shiga[1] in Japan, Kruse[2] in Germany, and Flexner[3] in the Philippines, have described a peculiar bacillus as the exciting cause of non-tropic epidemic dysentery. These bacilli are found as plump rods in the purulent and mucoid portions of the stool, sometimes in almost pure cultures, and often within pus-cells. Shiga's and Kruse's bacillus coincide in the essential feature, but Flexner's organism, though closely related, presents some distinctive features. The clinical significance of this distinction is thus far of no more importance than the differentiation between the typhoid and paratyphoid bacilli. [This whole subject has been carefully reviewed by Flexner in Albutt's System of Medicine, vol. ii, part ii, p. 495 et seq. Herter[4] agrees with the author and similarly objects to the term "paradysentery bacillus," because it appears to have been shown that the lesions caused by these bacteria are identical with those caused by the Shiga bacilli. Further, he says: "The Shiga bacilli are the cause of the severe epidemics of Japan and of Germany, but in the latter country bear the name of Kruse. The Flexner bacilli are apparently the cause of dysentery in young children much more frequently than the Shiga bacilli. . . . The Shiga and Flexner organisms, however, taken together, do not quite cover the entire range of bacillary dysentery; for, as Park and His have shown, there are pathogenic bacteria intermediate in type between the two. . . . Shiga[5] has lately adopted the classification of His, which recognizes four groups based on fermentative characters, and has added to this a fifth, intermediate between the acid bacilli and the non-acid bacilli."—Ed.] To avoid any prejudice, it is usual to speak of a Shiga-Kruse type and of a Flexner type of dysentery bacillus. They grow readily upon artificial culture-media, forming firm, non-liquefying, leaf-like colonies upon gelatin plates within twenty-four to forty-eight hours, which closely resemble typhoid colonies. According to Kruse, they are found in such large numbers in the fresh stools of dysentery that in plate cultures their colonies greatly exceed those of the colon bacilli. Like typhoid bacilli, they grow upon glucose agar either superficially or in the depths, without producing gas. Upon potato there is a yellowish growth along the line of inoculation, surrounded by a clear area. In bouillon they produce a uniform turbidity, with a sediment but without a scum, and without the formation of indol. (See p. 538.) They grow upon milk without curdling it. They behave like typhoid bacilli in litmus whey, and do not change neutral red agar. Their cultures upon agar develop a very characteristic sperm-like odor. They may be differentiated from typhoid bacilli, which they resemble so closely, by their plumpness and also by their lack of motility and the absence of cilia. They do not stain by Gram's method. They sometimes exhibit distinct polar granules. Kruse believes that the relation of these micro-organisms to dysentery is shown by the fact that they are agglutinated by the blood-serum of a dysenteric patient in a dilution of 1:50, and sometimes by a dilution of even 1:1000. Under certain conditions the agglutinative power of the serum of a dysenteric convalescent may last for a year. In reference to the diagnostic value of the agglutinative reaction, the reader is referred to Lentz's[6] article, as well as that of Kolle and Hetsch.[7] There is little danger of confusing typhoid and dysentery bacilli from any given case, because the clinical pictures of the disease they excite are so different. The significance of the bacteriologic examination of the stools in dysentery may best be expresed by saying that, in case not all the bacteriologic distinctions can be made, the demonstration of typhoid-like bacilli in the stools of a case showing the symptom-complex of dysentery argues for a bacillary dysentery.

Streptococci.—A number of serious diseases have recently been attributed[8] to an invasion of the digestive tract by streptococci. Their course is like that of

[1] Centralbl. f. Bakt., 1898, vol. xxiii, p. 599.
[2] Deut. med. Woch., 1900, p. 637.
[3] Phila. Med. Jour., 1900, vol. vi, p. 414.
[4] Infections of the Digestive Tract, p. 173.
[5] The Philippine Jour. of Sci., 1906, i, p. 485.
[6] Zeit. f. Hyg. u. Infectionskrankh., 1902, vol. xli, part 3, p. 559.
[7] Kolle and Hetsch, Experimentelle Bacteriologie, 1906.
[8] Compare, *e. g.*, Contribution à l'étude du streptocoque et de l'enterite streptococcique. Quatre mémoires par MM. de Cérenville, Tavel, Eguet et Krummbein, Ann. Suisses de méd., Series II, 1895. C. Sallmann, Basel.

typhoid, cholera, or, finally, of an acute enteritis with septicopyemic localization (peritonitis, endocarditis, nephritis, etc.). These cases can be easily diagnosed from a microscopic examination of the diarrheal stools, which always contain very extraordinary quantities of streptococci. They may be found in a dry preparation stained with carbolfuchsin or by Gram's method (See p. 715.) The vomitus and the urine may sometimes contain abundant streptococci. The prognosis in these cases is usually fatal, except in those resembling typhoid, which generally recover. (See pictures of streptococci, Fig. 284.)

Pneumococci.—According to the author's experience, Fraenkel's pneumococcus (see Fig. 281, p. 716) is a frequent cause of intestinal infection, which is evidenced at times merely by a febrile reaction, at times by pronounced symptoms of enteritis. The diagnosis is made by finding large numbers of the characteristic Gram-positive diplococci in the stools.

Anthrax Bacilli.—Anthrax can sometimes be diagnosed by the presence of anthrax bacilli in the loose, frequently bloody, stools. (See Fig. 309.)

[For further information upon the subject of intestinal bacteria the reader is urged to consult Herter, The Common Bacterial Infections of the Digestive Tract and the Intoxications Arising from Them.—Ed.]

CHARACTERISTIC NATURE OF THE STOOLS IN SOME DISEASES

Stools of Typhoid Fever.—Typhoid fever is generally accompanied by loose yellow stools of the consistence of pea-soup. They usually settle in layers, with a thick, granular sediment and a supernatant, cloudy, watery menstruum. The odor is generally very strong and offensive, and possibly diagnostic. The reaction is usually strongly alkaline. In fact, the stools generally contain abundant microscopic crystals of triple phosphates (ammoniomagnesium phosphate; see Figs. 256 and 257). Simple microscopic examination does not disclose any special bacteriologic characteristic. Typhoid bacilli can only be demonstrated by intricate and time-consuming culture methods. The stools are sometimes stained with blood. A slight tinge not infrequently precedes a profuse intestinal hemorrhage, and, hence, is to be carefully watched for. Pus in quantities which can be demonstrated microscopically is contained only in the stools of cases with severe and extensive ulcerations. The diarrheal stools of typhoid are usually very copious. Solid stools occur not infrequently, not only in the beginning, but even throughout the entire duration of the disease.

Stools of Asiatic Cholera and Cholera Nostras.—In mild attacks of Asiatic cholera and cholera nostras the stools may present the character of an ordinary diarrhea. In severe cases they are no longer fecal in color, but are thin and nearly colorless or grayish, like water in which tiny cloudy flakes are suspended (rice-water stools). The absence of any brown coloration is probably due to oligocholia or acholia. The stools no longer emit a fecal, but an insipid, semen-like odor. The reaction is alkaline or neutral. In the mucous flakes we see, under the microscope, intestinal epithelium arranged in layers, more or less abundant cholera bacilli (Fig. 231), and sometimes drops of fat. The stools may also be slightly tinged with blood, like meat-water. Cholera stools contain only about 2 per cent. of solids; of this, a large amount is sodium chlorid, and but very little proteins. The stools are usually very profuse, unlike those of dysentery, and are voided without any especial effort. As the general condition improves, they gradually resume a fecal appearance. As is well known, cases of cholera do occur without diarrhea (cholera sicca).

The stools of *cholera nostras* are much like those in true cholera, except that true cholera bacilli are absent, and that, corresponding to the milder nature of the disease, they are more or less stained by bile. Both the stools and vomitus in cholera nostras contain very varied micro-organisms (Finkler-Prior bacilli, streptococci, and others, see pp. 535 and 539).

Stools of Dysentery and Carcinoma of the Rectum.—Dysentery stools present the character of rectal diarrhea (see p. 511), *i. e.*, they are not profuse, but voided so much the oftener. Soon after the attack begins they lose their fecal character, and are at first slimy, then mucopurulent, and finally sanguinopurulent or serosanguinolent (meat-juice stools, white flux, red flux). We may often see peculiar solid, reddish or white fragments, which consist partly of blood-stained mucus (carunculæ of older writers) and partly of macroscopically visible particles of desquamated necrotic mucosa. The stools in dysentery may be practically odorless, but in grave cases (gangrenous flux) they emit a noticeable cadaverous odor. See pp. 519 and 539 in regard to the presence of dysentery bacilli (epidemic dysentery) and of amebæ (tropical dysentery and certain cases of common sporadic dysentery).

The stools of carcinoma of the rectum sometimes very closely resemble those of dysentery.

Stools in Diseases of the Pancreas.—Considering the prominent part played by the pancreas in the digestion of fats, it is easily understood that in some of the diseases of this organ which lead to its destruction or to the occlusion of its ducts, so-called "*fat-stools*" are observed. The latter are characterized macroscopically, microscopically, and chemically by their abnormal content of fat (steatorrhea). We must, however, be rather cautious in making use of this symptom for diagnosis, because, on the one hand, the stools may show an abnormal amount of fat in any case of marked icterus, and, on the other hand, cases of almost total destruction of the pancreas have been observed when the stools at the time showed no abnormal amount of fat. This is because emulsified fat, even without any pancreatic juice, can be very readily absorbed, as shown on p. 530, while evidently the fat not in emulsion is taken care of by the vicarious action of the bile. Hence fatty stools are diagnostic of pancreatic disorders only where there is no jaundice, and hence also the absence of fatty stools does not exclude destructive pancreatic disturbance. In making a diagnosis of pancreatic disturbance from the appearance of the stools we must also remember that, if the pancreatic juice be absent, chemical examination shows only insignificant quantities of soaps in the fatty stools (p. 544), the stools show but slight signs of putrefaction, and the urine contains only a slight amount of indican. (See p. 579.) Upon a mixed diet the stools contain a considerable amount of isolated muscle-fibers; and if raw meat has been eaten, these fibers show, according to A. Schmidt, preserved nuclei, provided the pancreatic function is entirely wanting. Larger pieces of muscle tissue are found only if the gastric digestion also is disturbed, so that the connective tissue is not dissolved. In pancreatic disease, where there is no flow of pancreatic juice into the intestines, well-hardened glutoid capsules (see p. 506 et seq.) are found undissolved in the intestinal contents, providing the gastric motility be normal. The iodoform-glutoid reaction is therefore absent. See also the demonstration of trypsin in the feces (p. 542 et seq.). Under certain circumstances a negative test for this ferment must be considered in the diagnosis of pancreatic disease.

CHEMICAL EXAMINATION OF THE FECES

REACTION OF THE STOOLS

Under normal conditions the reaction of the feces may be neutral, faintly acid, or faintly alkaline. Gamgee, as well as Nothnagel, considers a faintly alkaline reaction the most frequent. At any rate, under normal digestive and nutritional conditions, the reaction is not far from neutral. The reaction on the surface of formed feces often differs from that in the interior. The reaction may also change upon prolonged standing; it should, therefore, be tried on fresh stools. An admixture of urine will very soon produce an alkaline reaction. Pathologically, the reaction may become either strongly acid or strongly alkaline, according to the kind of decomposition processes which are occurring in the intestinal canal. Typhoid and cholera stools are usually alkaline. The stools of a patient upon a milk or a starch diet are usually, but not always, acid in reaction. The absence of gastric juice (achylia) curiously enough does not affect the reaction of the feces. Deficiency in bile produces acid stools.

PIGMENTS OF THE FECES

The color of the feces of normal adults is never due to unchanged bile-pigment (bilirubin), because the latter is transformed into urobilin in the intestine, and partly reabsorbed and used over again in the organism (probably to help form bile and to produce urinary pigment). Therefore the presence of bilirubin in the feces always indicates some abnormal function of the intestine—either some disturbance in absorption or in the chemical processes, or else some increased peristalsis. Bile-pigment often appears in diarrheal stools. It can then sometimes be recognized by its intense yellowish or greenish shade. Chemically, it can be very easily demonstrated by Gmelin's test (p. 575), *i. e.*, by dropping a little fuming nitric acid directly

upon the feces and noting the green, red, and violet rings around the drops of acid. The green ring is the most characteristic.

The normal pigment of stools is *urobilin* or *hydrobilirubin*, also called *stercobilirubin*. This substance may be easily extracted from the feces by means of alcohol containing hydrochloric acid, and then demonstrated in solution spectroscopically or chemically with zinc chlorid. (See Examination of the Urine, p. 584.) Ad. Schmidt recently described a simple method of demonstrating urobilin in the feces directly without extraction.[1] He adds a little concentrated mercuric chlorid solution to a small amount of feces in a porcelain dish. If urobilin be present, the feces will turn red. The reaction can be completed in about a quarter of an hour. The same test can be employed to demonstrate the presence of bilirubin, which will turn green in the presence of the mercuric chlorid solution. In the same specimen of feces we can therefore recognize, by the contrast of color, the particles which contain bilirubin and those which contain urobilin. Concerning the value of this reaction, the author has serious doubts, since, so far as he knows, it has never been demonstrated with pure solutions of urobilin, and since alkalis precipitate red mercuric oxid from solutions of mercuric chlorid, a fact which might lead to confusion if the stool were alkaline. Should disodium phosphate be present besides monosodium phosphate, it is quite conceivable that mercuric chlorid might precipitate mercuric oxid, even if the stool were acid or neutral in reaction. One observation of the author's tends to confirm this: a neutral stool gave Schmidt's reaction, although the very delicate zinc chlorid test (see above) showed no urobilin. The author, therefore, recommends the latter test (p. 584 et seq.) as used in the examination of the urine in place of Schmidt's reaction to demonstrate urobilin and Gmelin's reaction to test for unchanged bile-pigments (p. 575).

The demonstration of urobilin in the stools is of clinical importance in deciding whether in any given case of jaundice the common bile-duct is still partially patent; for in complete obstruction urobilin is absent from the feces.

BILE ACIDS IN THE FECES

Normally, the bile acids are almost completely reabsorbed from the intestinal canal, so that in the feces only small quantities of cholic and cholodinic acid are to be found. Very little is definitely known about the presence of bile acids in the feces under pathologic conditions. Their detection is a complicated process. (See Hoppe-Seyler, Physiologisch- und pathologisch-chemische Analyse, 1893, p. 47.)

DIGESTIVE ENZYMES IN THE FECES

The enzymes may be extracted from the feces by means of glycerin or bits of fibrin, which absorb the enzymes physically. Antiseptic substances must, however, be added to prevent putrefaction. Thymol, chloroform, oleum menthæ piperitæ, and oleum sinapis volatile are well adapted for this purpose. About one-half volume of a saturated aqueous solution of one of these substances is added to the feces to be extracted. The presence of the enzyme can then be demonstrated by an artificial digestive test. To some digestive mixture we add a little of the glycerin extract, or of the fibrin containing the enzymes. In the latter case the fibrin itself may serve as the object to be digested, or discs of coagulated egg-albumen (see p. 465) may be used. These digestive tests also require the presence of small amounts of antiseptic substances, so as to exclude the action of bacteria. At the conclusion of a digestive experiment we must examine microscopically to exclude any bacterial action. The action of pepsin is to be tested in a 0.2 per cent. solution of HCl, that of trypsin in 0.3 to 0.4 per cent. solution of Na_2CO_3. Arthus' method of testing for trypsin may be employed (p. 509). Both pepsin and trypsin seem normally to be destroyed in the intestine.

Von Jaksch generally found diastase and an inverting ferment in children's feces. Leo found the same in adults'. Neither author was able to demonstrate the presence of trypsin in most cases, but Leo demonstrated all three ferments in cases of diarrhea. E. Müller [2] has endeavored to obtain information regarding the amount of trypsin in the intestine by taking particles of the feces obtained after the administration of a cathartic and placing them on coagulated bovine or goat serum in Petri dishes. The proteolytic action is seen by the liquefaction of the area around the particles. The action of bacteria is excluded by keeping the dishes at 55°–60°. In order to be quite certain that the proteolytic action is due to intestinal ferments,

[1] Verhandl. des. Cong. f. inn. Med., 1895.
[2] Deut. Arch. klin. Med., 1908, xcii, 199.

one must eliminate the action of the leukocytic ferments. This may be done by using the serum of cold-blooded animals, *e. g.*, turtles, which contains an antibody to the leukocytic ferment, but which does not inhibit trypsin. Without this control a positive result is of no value in indicating the efficiency of the pancreatic digestion, and thus the method loses in its usefulness.

In a similar way Müller [1] uses starch plates to demonstrate pancreatic ferments in the feces, but it has been shown that the diastatic action still persists, although to much less degree, when the duct is completely occluded.

MUCIN IN THE FECES

Stools normally contain considerable mucin, which is increased in catarrhal conditions of the intestines. Sometimes the appearance and consistence of the feces (see p. 511 et seq.) are enough to show this. According to Hoppe-Seyler, mucin can be demonstrated chemically by mixing the feces with water, adding an equal volume of lime-water in which mucin is soluble, and then adding dilute acetic acid to the filtrate. Cloudiness indicates mucin.

Strassburger and Schmidt point out that this test is not sufficient, for nucleo-albumin gives a similar reaction, and it is necessary to show that the precipitate is free from phosphorus. The substance ought to reduce an alkaline copper solution after it has been digested for some time with 7.5 per cent. hydrochloric acid. Practically the differentiation has no significance.

PROTEIN AND PEPTONE OR PROTEOSES IN THE FECES

The detection of these substances by means of the biuret reaction must be performed with special caution, because the urobilin which is contained in the feces also reacts to this test (extracting urobilin with alcohol; see p. 569). Normal feces are free from any soluble proteins, peptones, and proteoses, but they can be demonstrated under pathologic conditions, especially diarrhea.

Schlossman [2] dilutes the feces with water, filters, precipitates the nucleoproteins and mucin by the addition of 30 per cent. acetic acid, filters again, and tests for proteins by the heat coagulation test, using sodium chlorid, the potassium ferrocyanid test, or the nitric acid test. (See Section on Urine, p. 563.)

CARBOHYDRATES IN THE FECES

Unaltered starch is best demonstrated microscopically. (See p. 530 and Fig. 201, *i–n*, p. 428.)

To show the presence of sugar, feces are boiled with water, then filtered, and the filtrate tested by Trommer's test or by the phenylhydrazin test (pp. 587 and 591). See also the Schmidt-Strassburger fermentation test (p. 532 et seq.).

QUANTITATIVE AND QUALITATIVE TESTS FOR FATS, FATTY ACIDS, AND SOAPS IN THE FECES

Even a microscopic examination of the stool will enable one to form some estimate of the content of fat (p. 530).

If it be desired to estimate the total amount of fatty substances (fats, fatty acids, and soaps), the Liebermann-Szekely method may be used (Pflüger's Arch., vol. lxii, 360, 1898). The feces are boiled with 30 per cent. potassium hydroxid until all the fats are saponified. The fatty acids are set free with sulphuric acid, dissolved in petroleum ether and alcohol, and titrated with alcoholic potassium hydroxid, using phenolphthalein as an indicator.

To estimate the amount of neutral fat, fatty acids, and soap separately [3] a weighed amount of the stool is dried at 100° C., then mixed with several times the quantity of sand, which has been treated for several days previously with water, alcohol, and HCl, and then again with water. The feces-sand mixture is now extracted with ether, by means of Soxhlet's apparatus, until no more fat can be removed. This

[1] Centralbl. f. inn. Med., 1908, No. 16.

[2] Schlossman, Zeit. f. klin. Med., vol. xl, parts 3 and 4.

[3] See Fried. Müller, Untersuchungen über den Icterus, Zeit. f. klin. Med., 1887, vol. xii, p. 51; Deucher, Correspondenzbl. f. Schweizer Aerzte, 1898, No. 11. Volhard's work upon the lipolytic ferment of the stomach should be consulted for the method of estimating the neutral fats and the free fatty acids separately (Zeit. f. klin. Med., 1901, vol. xliii, p. 417).

usually requires between eight and ten hours. The ether residue after thorough washing with warm water indicates by its weight the amount of neutral fats and fatty acids which are present. The content of fatty acids is determined by dissolving a weighed amount of the ethereal residue in alcohol and ether and then titrating with alcoholic potassium hydroxid, with phenolphthalein as an indicator. The amount so determined is subtracted from the total obtained from that in the ether residue, the result being the neutral fat.

To determine the amount of the soaps, the feces are boiled with acidulated (HCl) alcohol, after they have been first extracted with ether in the manner mentioned above; they are then dried again and extracted once more with ether. The hydrochloric acid will free the fatty acids from the soaps, and the latter may then be titrated in the second ether extract as described above. The amount of soap present may now be calculated from the amount of fatty acids. F. Müller has suggested a simpler method when we wish to determine only the neutral fats and the fatty acids, including the soaps (*i. e.*, the split fats). He advises boiling the dried specimen directly with acidulated alcohol, in order to liberate the fatty acids from the soaps. The feces will then contain only fatty acids and neutral fats. The former can be titrated as above in a definite portion of the ether extract.

With these quantitative estimates as a basis, it is easy to determine the total amount of fatty substances as well as the quantitative variations of the free fatty acids and soaps as compared with the neutral fats. The greatest amount of fatty substance is found in the stools in jaundice. In pancreatic disease the total amount of fatty substances in the stools is frequently increased, though this is not necessarily the case. In healthy individuals, and even in cases of jaundice, provided the pancreatic juice flows into the intestine, by far the greater part (84.3 per cent., F. Müller) of the fat is split up into fatty acids or soaps. If the pancreatic duct be occluded, Müller found only 39 per cent. of the fats split up, as against Deucher, who found 80 per cent. According to Deucher, the 80 per cent. is composed almost exclusively of free fatty acids, not soaps. More recent investigations of Brugsch[1] confirm Deucher's results. Bidert[2] has shown that the stool of dyspeptic infants suffering from fatty diarrhea contains as high as 53 per cent. of fat, excluding the soaps present.

CHEMICAL AND SPECTROSCOPIC TESTS FOR BLOOD IN THE FECES

Blood undergoes a variety of chemical changes during its passage through the digestive tract. The most important derivatives which originate from the hemoglobin are methemoglobin and hematin. As these derivatives are stable, and the iron contained in them may be demonstrated chemically (p. 546), while the erythrocytes are rapidly disintegrated in the intestine, except when an excessive hemorrhage has taken place, the chemical and spectroscopic tests for the pigments are much more accurate than the microscopic examination.

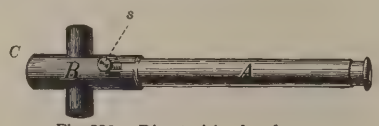


Fig. 232.—Direct-vision hand spectroscope.

Teichmann's hemin test and *Schönbein-Almén's turpentine-guaiac test* are the most useful for detecting chemically the hemoglobin derivatives in the feces. (See p. 573.) These methods often give positive results even when the microscopic examination for blood-corpuscles fails.

One difficulty in utilizing the turpentine-guaiac test in such complicated mixtures as the feces and the gastric contents is that, according to Weber,[3] many other substances can produce the bluish coloration of the reagent (see below). By employing the acidulated ethereal extract, Weber claims to avoid this difficulty to some extent: A generous sample of the feces or stomach-contents is rubbed up with water to which has been added one-third its volume of glacial acetic acid. The mixture is then shaken with ether. A little alcohol will hasten

[1] Brugsch, Zeit. f. klin. Med., lviii, parts 5 and 6.
[2] Jahrb. f. Kinderheilk., 1879, xiv, p. 336, and 1888, xxviii, p. 21.
[3] Berlin. klin. Woch., 1893, No. 19.

the clarifying of this ether extract. A few cubic centimeters are poured off, and 10 drops of a freshly prepared tincture of guaiac and 20 to 30 drops of old, so-called ozonized oil of turpentine are added. The green coating which forms on guaiac resin on exposure to air must be removed by scraping before the alcoholic solution is prepared. If blood be present, the mixture will turn violet blue; if not, it turns red brown, with often a slightly greenish tinge. The reaction is more marked if we add some water and then extract the blue pigment with chloroform. In healthy individuals the feces never react positively to this test unless the diet contain an

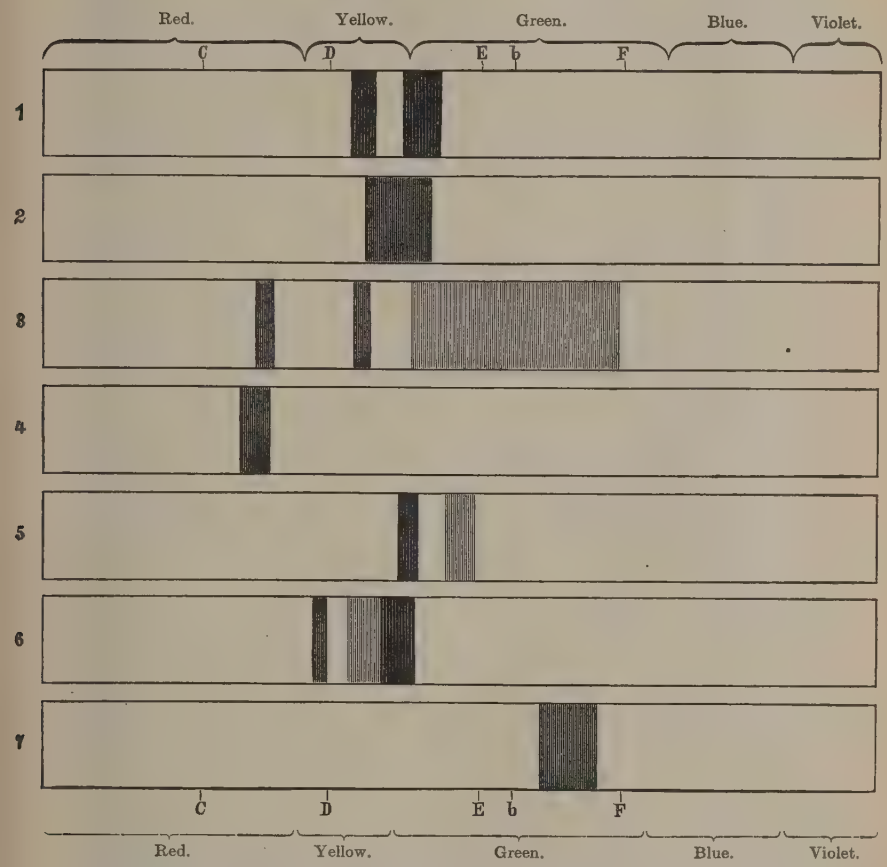


Fig. 233.—Important clinical spectra: 1, Oxyhemoglobin; 2, reduced hemoglobin; 3, methemoglobin; 4, hematin in acid alcoholic solution; 5, reduced hematin in alkaline solution; 6, hematoporphyrin in acid solution; 7, urobilin (after Salkowski).

excess of meat (see below). Weber found the test sensitive enough to demonstrate blood-pigment in the daily movement of a healthy individual after the ingestion of only 3 cm. of blood. Sources of error inherent in the method are mentioned below.

According to Boas,[1] the guaiac test for blood does not always yield decisive results in the examination of the feces, since the blue color is often veiled by the brown shades and rendered indistinct. For this reason Boas recommends a control test with aloin, as suggested by Klunge, Schär, and Rossel. According to

[1] Deut. med. Woch., 1903, No. 47.

Rossel,[1] the test is performed as follows: 5 cc. of the stool are extracted with 20 cc. of ether, in order to remove the fat, which would subsequently interfere with the test by the formation of emulsions. After the removal of the ether, 3 to 5 cc. of acetic acid are added to the feces, and the mixture is again extracted with ether in a test-tube. The acid ethereal extract obtained in this manner is then employed for the investigation. A solution of aloin is prepared by dissolving as much aloin as can be placed upon the point of a small knife in from 3 to 5 cc. of 60 to 70 per cent. alcohol. To the acetic acid ethereal extract is first added, 20 to 30 drops of a resinous oil of turpentine, and then 10 to 15 drops of the solution of aloin; if the stool contain blood, the resulting mixture soon becomes bright red, and upon standing for a time assumes a cherry color. If no blood be present, the aloin solution remains yellow for at least one to two hours, and then acquires a slightly reddish tinge. According to Boas, the aloin reaction may be markedly accelerated or made more distinct by the addition of a few drops of chloroform. With this modification, agitation of the mixture results in the formation of reddish droplets which settle in the bottom of the tube as an intense red precipitate. Under certain conditions Boas regards the aloin test as more sensitive than the guaiac test. According to Brandberg, the oil of turpentine may be replaced by a dilute solution of hydrogen dioxid.

Adler's Benzidin Test for Blood.—O. and R. Adler, Schumm and Westphal, Schlesinger and Holst[2] recommend benzidin for testing for blood in the stools. Cohnheim[3] recommends the following procedure. A small amount of benzidin purissimum (Merck) is dissolved in 2 to 3 cc. of acetic acid. Ten to 12 drops of this solution are poured into 2 cc. of commercial hydrogen dioxid containing 3 per cent. H_2O_2 by weight. A small amount of the feces are boiled with 5 to 6 cc. of water, and after cooling a few drops of the extract are added to the hydrogen dioxid-benzidin solution. In the presence of blood, a blue color is produced after one to three minutes. According to Citron, the test is better performed by using the extract of the feces made with acid ether. A small amount of the feces are extracted wth glacial acetic acid and ether. To the extract a small amount of benzidin is added, and a few drops of hydrogen dioxid. In the presence of blood the mixture turns green.

Errors in the Detection of Blood.—The above methods for the detection of blood are extremely sensitive, but must be accepted only with certain reservations. They all depend on the presence of a catalyzing agent in the stools, which, in the presence of old oil of turpentine or hydrogen dioxid, sets free nascent oxygen. The reaction is called a superoxydase action. Other substances than blood give the reaction—the hemoglobin derivatives of the muscle tissue of the food, the chlorophyll of plant food, certain plant and animal ferments, and salts of iron and bismuth. Part of these are excluded by employing the ether extract of the feces. It appears, however, that certain salts of iron and bismuth are slightly soluble in ether and complicate the results. In order to avoid this it is necessary to be sure that, for a time before the test has been made, the patient has not received either of the two above-mentioned drugs. Plant and animal ferments do not interfere with the reaction, as they are not soluble in the ethereal extract. On the other hand, the hemoglobin of meat acts in exactly the same way as the blood from the intestinal tract, and it is necessary, in performing the test, to exclude meat from the diet for several days before the test is made, so that at least two stools have been passed after the meat has been withdrawn.

The Spectroscopic Detection of the Derivatives of Blood-pigment.—An ordinary hand spectroscope (direct vision, after Browning, Fig. 232) is sufficient for this purpose. The material to be tested must be well diluted with water and examined by transmitted sunlight or in daylight. The spectroscope should first be adjusted by moving the inner tube, so that Fraunhofer's lines can be distinctly seen if the instrument be pointed toward a white surface or the sky. In order to avoid side lights and to make an examination with an ordinary test-tube the author employs the cap *B* (see Fig. 232), made of brass and blackened on the inside. This can be shoved over the prism end of the spectroscope, and fastened by means of the screw, *s*. The test-tube, with the substance to be examined, is placed in the cross-tube *C*, and the light is admitted through *B*.

The normal pigments of the feces, even if considerable blood be admixed, frequently mask the characteristic spectrum of the hemoglobin derivatives by their

[1] Arch. f. klin. Med., 1903, vol. lxxvi, p. 505.

[2] O. and R. Adler, Zeit. f. physiol. Chem, 1904, p. 41, parts 1 and 2, p. 59; O. Schumm and C. Westphal, ibid., 1906, vol. xlvi, parts 5 and 6, p. 510. Schlessinger and Holst, Münch. med. Woch., 1907, No. 10.

[3] Die Krankheiten der Verdauungsorgane, Berlin, Karger, 1908.

diffuse absorption of light; hence a mere watery dilution of the feces is not to be recommended in doubtful cases. The following method is more desirable: Several cubic centimeters of the stool to be examined are mixed with water and acidulated with several drops of sulphuric acid until the Congo-red reaction is marked. (See p. 450.) The mixture is then filtered, and the filtrate extracted with ether. If the ether does not separate properly, the extraction may be hastened by adding a few drops of alcohol. If the feces contain blood, the ether turns reddish brown and shows spectroscopically the characteristic bands of acid hematin in the red. (See Fig. 233.)

Of course, the hemoglobin of muscle-fiber gives the same reaction and the same spectrum as the hemoglobin of blood, so that we must be careful to exclude any mistake by seeing that the patient does not ingest any large amount of raw or half-cooked meat.

SIGNIFICANCE OF THE DETECTION OF BLOOD IN THE FECES

The significance of the presence of extremely small amounts of blood in the feces is very great, in the early diagnosis of cancer of the stomach or of the intestines, ulcers of the stomach, tuberculosis of the intestines, typhoid fever, and other conditions of the digestive tract associated with hemorrhage. Boas[1] has shown that in cancer of the stomach constant occult hemorrhages occur. This is of importance not only as a diagnostic sign, but as indicating the cause of the cachexia and anemia of these patients. It is very noteworthy, however, that in pernicious anemia one also has the constant presence of occult amounts of blood in the stools. This complicates the differential diagnosis between this condition and that of carcinoma of the stomach. [Most of the recent literature upon this subject has been reviewed by White,[2] in a very comprehensive paper to which the reader is referred. He compared the value of the Weber guaiac test with "hydrogen dioxid (see above, Brandberg's modification) and the Schlesinger and Holst benzidin test; 95 per cent. of of his positive results were in cases of cancer or ulcer of the esophagus, stomach, or bowel. One hundred and six examinations of the feces with the benzidin test in 88 cases, including healthy persons on a meat-free diet, neuroses of the esophagus, functional diseases of the stomach and bowel, chronic gastric and intestinal catarrh, gallstones, syphilis, and cyst of the liver, gave only negative results; 48 examinations of the feces in 15 cases of acute or chronic ulcer of the stomach or bowel or hepatic cirrhosis gave intermittent positive and negative results; 20 examinations of feces in 8 cases of cancer of the esophagus, stomach, or bowel gave only positive results. . . .

"One hundred and eight examinations of feces in the 88 meat-free and non-ulcerative cases gave identical negative results with the two tests; 20 examinations of feces in the 9 cancer cases gave identical positive results; 30 examinations of feces in the 9 cases comprising acute gastric and duodenal ulcer, ulcerative colitis, and cirrhosis gave identical positive or negative results. Of the 46 positive tests with benzidin in 144 examinations of the feces of sick persons, all but 3 were positive with guaiac. Of the 87 positive tests with benzidin in sick persons (including results of 144 examinations of feces, and 131 examinations of gastric contents), all but 11 were positive also with guaiac.

"These 11 positive results with benzidin in sick persons (where the guaiac test was negative) are distributed as follows: 3 were examinations of feces and 2 of gastric contents in chronic ulcer, where the somewhat greater delicacy of the benzidin test was distinctly useful in diagnosis; 6 were examinations of gastric contents in cases where examination of the feces by both tests was negative. The fact that a few more positive results were obtained in the gastric contents in this class of cases with benzidin than with guaiac is not an important matter, as we place little value on a positive result in gastric contents after the use of a stomach-tube when the feces are negative. The objection that the benzidin test is too delicate for clinical work is removed by the use of the Schlesinger and Holst modification as far as my experience goes in the constant use of the test for almost two years.

"The chief advantages of the benzidin over the guaiac test are the greater value of a negative result in ruling out all hemorrhage, the much greater ease and rapidity of its performance, and the greater clearness of the color reaction in the feces.

"Those who wish at first to control their results with benzidin by means of the guaiac test will find a great amount of time saved by applying the benzidin test first; it takes only two minutes to perform, and a negative result renders any further test unnecessary."—Ed.]

[1] Boas, Deut. med. Woch., 1901, No. 20.

[2] Boston Med. and Surg. Jour., June 10, 1909, vol. clx, p. 733.

URINARY EXAMINATION

AMOUNT OF URINE

The daily volume of urine excreted by a healthy adult varies under average conditions between 1500 and 2000 cc.[1] An abundant ingestion of fluid will considerably increase, and a diminished ingestion of fluids or food will correspondingly diminish, the amount. The amount will vary in inverse ratio to the insensible perspiration; hot weather diminishes and cold weather increases the amount. Profuse perspiration, diarrhea, and vomiting all decidedly diminish the amount. In children or abnormally small individuals the daily amount of urine is correspondingly less. The normal average for such a person can be determined from the following formula, supposing the average weight of a healthy adult to be 75 kilos (165 pounds):

$$x : 1500\text{–}2000 :: a : 75,$$

where x represents the daily amount of urine sought and a the weight of the individual in kilos. Children, and especially nursing infants, on account of the preponderance of liquid in their food, excrete proportionally a larger amount of urine than is represented by the formula.

According to Martin and Ruge,[2] 67 per cent. of all new-born infants excrete urine the first day of life, but generally only after the lapse of twelve or more hours. The remaining 33 per cent. do not void urine until the second or the beginning of the third day. The daily amount of urine of the new-born varies between 150 and 200 cc. Rancke, Bischoff, and others estimate the excretion per diem from the third to the fifth year as about 700 cc.

As a rule, less urine is voided during the night than during the day.

According to Quincke,[3] this condition is reversed, *i. e.*, more urine is excreted during the night than during the day in heart and kidney diseases, in the aged with arteriosclerosis, in cachexia, and usually in diabetes insipidus. Under these conditions the amount voided at night may be double that voided during the day, as contrasted with the normal proportion of one-fourth to one-half as much. Not only the watery, but the solid, constituents as well are thus increased. Quincke regards this phenomenon as the result of a nocturnal recuperation of the damaged organs (heart and kidneys). It may, however, be considered as the result of a "*bradyuria*," *i. e.*, the water excretion may be delayed, assuming that the diseased kidneys react abnormally slowly, and not until night, with an increased diuresis, to the food and fluid ingested during the day.

THE COLLECTION OF URINE

[Much work has been done by clinicians, which, owing to the faulty methods in which the urine has been collected, has subsequently been proved to be worthless. This is particularly the case in examinations of the urine where a twenty-four-hour specimen has not been obtained. It may be said without reserve that a fractional specimen of urine is of

[1] [In this country the average quantity eliminated in twenty-four hours would fall considerably below this. The figures usually given are 1000 to 1500 cc.—Ed.]

[2] Vierordt, Daten und Tabellen, 1888.

[3] Arch. f. exp. Path. u. Pharm., vol. xxxii, parts 3 and 4.

no value for examination except for certain qualitative tests. These are: specific gravity, reaction, presence of albumin, indican, glucose, urobilin, acetone, and for microscopic examination. These may properly be performed with a small specimen of urine. All quantitative tests made with a sample of urine of which the twenty-four-hour quantity is not accurately known are useless. Unfortunately, they are also worse than useless, for they may lead the clinician to use the results so obtained for diagnosis which are based on entirely wrong premises. It must be pointed out that the fact that a urine contains 2 per cent. of urea, 4 per cent. of glucose, or 0.1 per cent. of albumin is of no importance except in so far as it shows that the urine contains urea, glucose, or albumin. What is of importance, however, is to know that a patient is excreting 30 gm. of urea, or 100 gm. of glucose, or 1.0 gm. of albumin in the twenty-four hours. This information is only to be obtained when a twenty-four-hour specimen of urine has been collected.

To obtain a definite twenty-four-hour specimen of urine, an hour should be fixed at which to start. It is best to start at 8.00 A. M. The patient should be instructed to urinate at this hour, and all urine passed at this time should be discarded. During the subsequent twenty-four hours all urine voided should be collected,[1] and at 8.00 A. M. the following morning the patient should be instructed to empty the bladder, and this should be added to what has already been collected. In this way the whole amount of the preceding day is obtained. The urine is most conveniently collected in wide-mouthed two-quart preserve jars fitted with a screw or patent top. A few cubic centimeters of chloroform should be placed in the jar before collecting the urine, and after each addition the contents of the bottle should be well shaken. It is well to keep the bottle in a cool place. No time should be lost in submitting the urine to examination after the collection is complete.

So much misdirected treatment has been made on the basis of statements based on the percentages of substances contained in the urine—statements which are completely inadequate—that it has seemed advisable to point out clearly the necessity of obtaining a complete twenty-four-hour specimen.

In view of what has been said regarding the influence of undernutrition on the composition of the urine, it is also of importance to know the composition of the food taken at the time the urine is collected. Information of this kind is of great significance when, either from a pathologic condition, or as the result of diet, the patient is losing weight. If the food be analyzed, particularly for its nitrogen content, one is able to ascertain whether a loss of weight is due to the consumption of fat and carbohydrate, or whether the muscle and other protein-containing tissues participate in the loss. In every instance treatment must be directed to guard against a loss of protein material to the body. This can only be done intelligently when the amounts of nitrogen in both food and excreta are determined, and the one balanced against the other. A concrete example of this will make the case clearer.

Any attempts to reduce weight in obesity by means of diet must be made with the idea in mind of preventing a loss of muscle tissue. The loss desired must be at the expense of the carbohydrate, and particularly

[1] The patient must be especially warned against loss of urine during defecation. Before going to stool the bladder should be completely emptied of urine.

of the fat. The diet in these cases must be so regulated that while loss of weight occurs, the balance between the intake and output of nitrogen must be zero. A loss of weight produced at the expense of protein material is harmful, and the measures producing it must be discontinued. The above information can only be obtained by a simultaneous analysis of the twenty-four-hour urine and the feces and of the total amount of food ingested during this time. If more nitrogen is found in the excreta than is present in the food, the diet must be so regulated that the loss is prevented. This is often to be accomplished by increasing the amount of protein, and at the same time decreasing the amount of fat and carbohydrate consumed.—C. G. L. W.]

Polyuria means an increase, *oliguria*, a diminution, in the quantity of urine.

The quantity of urine in pathologic conditions depends, first, upon the condition of the secreting renal parenchyma, and, second, upon the rapidity of the blood-current in the kidneys (Heidenhain). It is, therefore, affected by a general circulatory disturbance, as well as by disease of the kidneys alone. To alter it appreciably both kidneys must be diseased, for otherwise the healthy kidney would assume vicariously the total function, as regularly occurs after unilateral nephrectomy. The more acute the nephritis, the more the amount of urine falls below the normal; the more chronic the course of a nephritis, the more the amount exceeds the normal. Although as yet we have no definite explanation of the latter phenomenon, it is presumably due to a compensatory process.[1] This increase reaches a maximum in the true contracted kidney, where the volume has been found to be as high as 12 liters a day (Bartels). In regard to the amount of secretion, the so-called chronic parenchymatous nephritis resembles sometimes acute nephritis and sometimes the contracted kidney. A similar variation in amount is observed in amyloid kidney. Diseases of the heart and lungs, leading to passive congestion, are associated with a diminution in the amount of urinary excretion, which clearly depends upon a slowing of the renal circulation. In such disturbances the estimation of the amount of urine is, therefore, of great diagnostic and prognostic significance.

It was formerly believed that vasomotor influences alone were responsible for the variations in the amount of urine noted in certain psychic states, especially diabetes insipidus, in which the polyuria could be attributed to well-defined nervous influences, as well as convulsive seizures (especially in hysteria with so-called urina spastica) or attacks of angina pectoris. It is probable, however, that the quantity depends upon the influence of the nervous system on the urinary secretion. There has been no doubt of the existence of such influences, since the discovery, in renal epithelial cells, of nerve-endings which can be of secretory significance alone. Polyuria in diabetes insipidus is the most significant result of such nervous influences that has been observed. The daily quantity of urine may reach 30 quarts or more. Many other alterations in the volume of the urine depend upon quantitative and qualitative variations in the substances thus eliminated, and are primar-

[1] The increased blood-pressure is frequently assumed as an explanation of the polyuria in chronic nephritis. This assumption seems to the author unwarranted, since he has observed cases with long-continued polyuria without any elevation of blood-pressure, in which the autopsy revealed typical contracted kidneys and absolutely no trace of cardiac change.

ily induced by disturbances of metabolism, *e. g.*, the polyuria in diabetes mellitus, which, in the author's experience, has reached as high as 18½ quarts.

FREQUENCY OF URINATION

Although varying decidedly in different individuals, the frequency of urination corresponds in general to the amount of urine excreted. It is also influenced, however, by any inflammatory affection of the urinary tract or by any disturbance of innervation of the bladder. The increased frequency of urination (usually of less amounts than normal) from inflammatory conditions of the urinary tract depends upon a stimulation of the bladder reflexes (pollakiuria). It is generally accompanied by the subjective sensation of urgency (bladder tenesmus). Although observed chiefly in affections of the bladder, and especially of its neck or of the urethra, this frequent voiding of urine may depend also upon kidney disease, resulting either from a pathologic reflex emanating from the kidney, or from the irritation of an abnormal urine upon the mucous membrane of the bladder. Diseases of the spinal cord which either increase the irritability of the bladder or weaken the sphincter are also responsible for an increased frequency of urination. An abnormally infrequent urination depends upon some mechanical or nervous obstacle to the emptying of the bladder. (See later, Examination of the Nervous System, Innervation of the Bladder.)

SPECIFIC GRAVITY OF THE URINE

For the sake of simplicity the specific gravity of the urine is ordinarily expressed in four figures, taking the specific gravity of distilled water as 1000 instead of 1. Special aërometers called urinometers are employed for this purpose. Their scale is marked from 1000 to 1050. To insure a correct reading the subdivisions should be sufficiently wide apart. Many urinometers are not very accurately constructed, so that it is always well to compare a new instrument with a reliable one, or at least to ascertain whether it reads 1000 in distilled water at the ordinary room temperature, 15° C. (60° F.). Although a very large urinometer is more accurate, a smaller instrument requires less urine, which sometimes is a distinct advantage.

In the determination of the specific gravity the urine is poured into a tall glass cylinder [a urinometer and an appropriate glass cylinder are generally obtained together.—Ed.], the urinometer is immersed in the urine, and then, with the eye at the level of the surface of the urine, the subdivision which corresponds to the upper part of the curve of the meniscus is read off. For the sake of accuracy, the cylinder should be sufficiently large to allow the urinometer free motion. The bulb of the urinometer should not be allowed to stick against the side of the vessel, all bubbles or froth should be removed from the surface of the urine by means of filter-paper, and the urine should be at the ordinary room temperature. If the urine be colder than 15° C., one-third of the urinometer unit should be subtracted for every degree of Centigrade below the ordinary temperature; if warmer, the proportionate amount should be added. Ordinarily, such corrections are of slight significance, but they assume decided importance in diabetes insipidus and in other diseases accompanied by pronounced polyuria and a diminished specific gravity of the urine (chronic nephritis), because in such conditions the specific gravity of the urine is but slightly above that of water. In diabetes insipidus, for example, the influence of the temperature of the urine, if these corrections be not made, may mask the uniformity of the specific gravity characteristic of this affection. Since the specific gravity

of individual specimens of urine varies so decidedly during the day, it is imperative that the specific gravity of a mixed sample from the total twenty-four-hour secretion be obtained if any definite conclusions are to be drawn from the results concerning metabolism or the functions of the circulatory or secretory organs.

If the specimen be too small to work with in the ordinary way, it is a simple matter to dilute it with distilled water in a known proportion, to estimate the specific gravity of the mixture, and then to calculate the specific gravity of the urine, at least approximately.

The specific gravity of a twenty-four-hour specimen of urine varies normally from 1015 to 1020. Copious beer- or water-drinking may bring it as low as 1002; excessive perspiration and vigorous exercise as high as 1040. The variations in the ingestion of food and liquids, or in the loss of water from the skin or from the lungs, is responsible for the marked differences which occur in single specimens, as well as in the twenty-four-hour specimen.

Pathologically, the specific gravity is influenced by the secreting parenchyma of the kidney, by the velocity of the renal circulation, and by abnormalities of metabolism. The same factors which influence the amount of urine affect the specific gravity, but in the opposite manner, so that the specific gravity usually varies inversely with the amount of urine. Both under physiologic and pathologic conditions, therefore, a scanty urine is more concentrated than a profuse one. In acute nephritis the urine is concentrated and of a high specific gravity; in chronic nephritis, due to a true contracted kidney, the urine is profuse and of a low gravity. Diabetes mellitus forms an exception to the rule, since the excretion of sugar produces a high specific gravity despite the excessive amount of urine; this is so characteristic that a diagnosis is often possible on this ground alone. Some types of nephritis are also exceptions to the above rule, such as those showing a tendency to uremia and concomitant diminution in the excretion of solids; these cases present a low specific gravity with a small amount of urine. Again, in some cachectic conditions, even without nephritis, diminished metabolism and the lessened ingestion of food, as well as of water, produce a fall in volume of urine and, at the same time, a low specific gravity.

The urine in diabetes insipidus is especially characteristic. The urine has the extremely low specific gravity of 1005–1006, and the volume is correspondingly high—usually 3000–7000 cc. Occasionally, more than 30,000 cc. have been excreted in a day. If the amount of water be restricted, the specific gravity of the urine, as Strubell, Tallqvist, E. Meyer, and F. Seiler have shown, does not rise. This measure, which has been used for therapeutic purposes, gives rise to severe general disturbances, which seem allied to uremia, and, like this condition, seem to be dependent on a hyperosmotic condition of the blood. (See Examination of the Blood.) A full protein diet, which raises the specific gravity of the urine in healthy individuals from the increased urea formation does not have a decided influence on the specific gravity of the urine of patients suffering from diabetes insipidus. If the amount of water has been restricted, a retention of urea takes place. There is increased thirst, and only after the intake of a sufficient quantity of water does the patient eliminate the urea. In chronic nephritis associated with polyuria the kidney adapts itself better to the amount

of solids to be excreted than does the kidney in diabetes insipidus. But occasionally one sees a condition in the former disease which is very close to that of the latter.

The specific gravity is a fairly accurate indication of the amount of solids excreted in the urine. The solids excreted in 1 liter of urine can be approximately represented in grams by multiplying the last two figures of the specific gravity by 2.2337.[1] A urine of high specific gravity is called *concentrated*. The urea is mainly responsible for the specific gravity. For this reason alone, apart from the diminished secretion of water, a fever urine is always concentrated.

In reference to the value of the determination of the specific gravity of the urine as a substitute for the cryoscopic urinary examination, see p. 668.

TRANSPARENCY OF THE URINE

Freshly voided normal urine is absolutely clear and transparent, but after it has been standing for some time, an indistinct cloud of so-called mucin, "the nubecula," appears. (See p. 571.) Various other insoluble substances may cloud pathologic specimens of urine. (See the section on the Sediment and Turbidity of the Urine, p. 669 et seq.)

COLOR OF THE URINE

NORMAL URINARY PIGMENT

The color of the urine varies normally within different shades of yellow, the depth of color increasing in direct proportion to the specific gravity. The abundant urine of a drinker or of a person with contracted kidneys may be as pale as water, as contrasted with the scanty urine of acute nephritis, of passive congestion, or of fever, which is almost always dark. In diabetes mellitus, despite the high specific gravity, the urine is remarkably pale. This is of similar diagnostic importance as the great increase in amount. The urine in anemic individuals is always paler than normal, except in pernicious anemia. There the urine is quite dark, because this disease is associated with a rapid destruction of the red corpuscles, and, as is well known, the urinary pigments are derived from the hemoglobin.

The only method of designating the color of the urine is to compare it with certain fixed shades on a chart. In Neubauer and Vogel's book,[2] unfortunately, only a few different shades are represented. Radde's [3] scale can be used for other purposes as well, and is more highly recommended. Naturally, to obtain uniformity of results, a certain uniform thickness of the urine must be observed in each case, and the specimen must be held against a white background. For the quantitative determination of the normal urinary pigment (urochrome) see p. 612.

[1] Vierordt, Daten und Tabellen zum Gebrauch für Mediciner, 1888.

[2] Anleitung zur qualitativen und quantitativen Analyse des Harnes, older editions. In the more recent editions, edited by Huppert and Thomas, this plate is no longer included.

[3] Otto Radde, Stenochromatische Anstalt, Hamburg, 1877.

PATHOLOGIC URINARY PIGMENTS

Hemoglobinuria; Hematuria.—Urine which contains blood or hemoglobin presents a red, brownish-red, or sometimes even a greenish-black or black color. These variations depend partly upon the amount of admixed blood, and partly upon the degree of alteration of the blood-pigment in the urine. Urine containing hemoglobin proper is reddish, while that containing methemoglobin is more brownish. (See Spectroscopic Demonstration of Blood-pigment, p. 574 et seq.) Such urines are usually cloudy on account of the blood-corpuscles and other organic mixtures, and in hemoglobinuria on account of flakes of hemoglobin. Upon standing, these elements all settle in the form of a sediment.

Hematoporphyrinuria (see p. 575).—Urine which contains hematoporphyrin is sometimes excreted after persistent use of sulphonal, trional, or tetronal. Its color, if the layer of urine is thick, is a very dark brown or almost a black; and if thin a yellowish red to violet.

With **jaundice** the urine contains *bile-pigments*, and its color varies from a dark yellow or green to a brown or black, depending upon the concentration of the urine and the amount of bile-pigment, or upon its chemical modifications. When such a urine, especially if strongly acid, is allowed to stand in the cold for some time, needle-like crystals of bilirubin separate out and settle with the rest of the sediment. (See p. 679, Demonstration of Biliary Coloring-matter; also p. 575 et seq.) The urine of patients suffering with **melanotic tumor,** a very rare condition, contains *melanin* (*phymatorrhusin*). It becomes dark brown to black after prolonged exposure to the air, the melanin having separated from the "melanogen" of the urine. As a rule, the urine is perfectly clear, although it may rarely become cloudy from a granular precipitate of the melanin. (See Demonstration, p. 582 et seq.)

The large amount of **urobilin** in the urine of some varieties of icterus (cirrhosis) shows a similar dark-brown color. (See Reaction, p. 584 et seq.)

Various **aromatic products,** such as result from decomposition by putrefactive processes (peritonitis, suppuration, etc.), are often responsible for a remarkably dark-colored urine. This color is sometimes seen even in a freshly voided specimen, but more commonly appears after exposure to the oxidation of the air. Either *pyrocatechin*, *alkapton*, or *indican* may give rise to a dark-colored urine. If much indican be present, there is sometimes a conspicuous precipitation of indigo. (See pp. 581 and 679.) Although the bluish tinge of the indigo may be masked, indigo generally rises to the surface. (See Demonstration of Indigo by the color of the urine, a bluish-black scum, due to the separation of the Indican, p. 579 et seq.)

Indigo may be formed from indican even before the urine is voided. The author once obtained a specimen of grass-green urine from an apparently healthy boy without being able to determine the precise condition. The chloroform extract showed that the color depended upon the admixture of the blue of the indigo with the yellow of the urine.

MEDICINAL SUBSTANCES WHICH COLOR THE URINE

There are so many drugs which may be responsible for an abnormal color of the urine that it is possible to mention here only the most important. At the same time the author wishes to emphasize the fact

that, if the urine show any peculiar or extraordinary color not otherwise explainable, we should consider the possibility of attributing it to the administration of some drug.

Carbolic acid, coal-tar products, hydroquinone, resorcinol, pyrocatechin, naphthalene, salol, the *arbutin* derived from the leaves of *Uva ursi,* and many other aromatic substances, when administered internally, and sometimes even when employed externally, produce a dark, olive-green to black urine. The dark color frequently becomes apparent only after considerable exposure to the air or after the urine becomes alkaline. It depends upon the formation of colored compounds by the oxidation of the excreted drugs. Hydroquinone and pyrocatechin are especially prone to result from such oxidations, and they cause the dark color of urines containing phenol, salol, and arbutin.

The appearance of this color in the urine should occasion no alarm unless one of these drugs is being used externally; as, for instance, in the old Lister antiseptic employment of carbolic acid. Then the drug is evidently being absorbed in considerable and uncontrollable amount, although not intended to be absorbed at all. As a product of excretion simply, the dark color is of no particular significance. The dread of it is largely due to the frequency with which it was met after the use of the carbolic spray of Lister's method. Often quite moderate doses of salol (2 gm., 30 gr., a day) will be accompanied by the excretion of a black urine without any ill effects, while doses large enough to cause toxic symptoms may cause no discoloration. These variations depend to a considerable extent upon the degree of acidity of the urine, as well as upon the length of time it is exposed to the air.

The administration of *chrysarobin, rhubarb, senna,* or *cascara* may produce a yellow or reddish-brown urine, which will become distinctly red if the reaction is alkaline. (This is due to the presence of chrysophanic acid; see p. 612.) *Santonin* is apt to produce a saffron-yellow or greenish color, which changes to red if the urine be rendered alkaline. (See Test for Santonin, p. 612.) The pigment of *madder,* of *beets,* and of *huckleberries* may, under certain conditions, be excreted in the urine (Gorup-Besanez).

ODOR OF THE URINE

Normal urine possesses a peculiar faint odor which is not particularly unpleasant. The disagreeable, so-called urinous odor depends upon bacterial decomposition taking place either in the urinary tract or after the voiding of the urine. It is often called ammoniacal, since ammonia can usually be demonstrated in such a specimen. There are, however, other odorous substances concerned besides ammonia, as one can appreciate by the sense of smell, *e. g.,* aromatic decomposition products (phenol). Decomposing albuminous urine presents an odor so characteristic as to justify a definite diagnosis of the presence of protein.

Decomposition in the urinary tract, or the absorption of hydrogen sulphid from putrefactive areas in the body, will sometimes produce an odor of sulphuretted hydrogen (hydrothionuria).

Various odorous substances, if introduced into the body, appear directly as such in the urine, *e. g.,* the odorous substances of valerian, leek, castor, crocus (saffron), asafetida, meat, bouillon, and coffee. Other substances, from characteristic odorous compounds in the body about which little is understood, but which are excreted in urine, *e. g.,* balsams, especially the balsam of copaiba, cubebs, saffron, and the oil of turpentine. Even small doses of the last impart a very distinct odor of violets. The peculiar odor of the urine after eating asparagus is due to methylmercaptan (Nencki).

REACTION OF THE URINE

Normal urine has an acid reaction, due not to free acid, but to acid salts, especially dihydrogen sodium phosphate, H_2NaPO_4. At times the reaction may be amphoteric, *i. e.*, the urine may turn blue litmus-paper red, and red paper a faint blue. This is due to the presence of the acid dihydrogen phosphate and the alkaline disodium phosphate in a definite relationship of such a nature that each salt is capable of exerting its influence upon the indicator without interference with the other. This is possible only provided the acid salt is not present in too great an excess.

Specimens of urine voided at different times of the day react differently, a variation depending largely upon the phenomena of digestion. During digestion the secretion of hydrochloric acid by the stomach diminishes the acidity of the urine, which may even become alkaline. This diminution of acidity is shown by a more ready precipitation of the earthy phosphates and carbonates, so that the urine is cloudy when first voided or when heated. The more hydrochloric acid secreted by the stomach, the more decidedly alkaline the urine simultaneously excreted, so that such a turbidity after eating oftentimes suggests a diagnosis of pathologic gastric hyperacidity. It is incorrect to consider the precipitation *per se* a manifestation of perverted metabolism inducing phosphaturia. If the acid contents of the stomach are vomited or removed by gastric lavage, the acidity may be still further reduced or the urine even rendered decidedly alkaline, although oftentimes without vomiting or lavage; the degree of hypersecretion alone is sufficient to cause quite a marked permanent phosphaturia and an alkaline urine. Perhaps the acid is excreted in the feces; but thus far we have no direct investigation of this point.

The nature of the food ingested will also alter the reaction of the urine. A vegetable diet or a liberal consumption of wine or of fruit may cause the excretion of an alkaline urine; the alkalinity is occasioned by the fact that the organic acids become oxidized in the body to alkaline carbonates. On the other hand, a diet rich in protein or meat will intensify the acid reaction, because acids, especially sulphuric acid, result from the oxidation of protein in the organism.

Alkaline drugs render the urine alkaline. All acids not oxidized to carbonic acid, *e. g.*, the mineral and aromatic acids, intensify its acidity. Most of the fatty series are oxidized to carbonic acid, and so, in moderate doses, do not usually increase the acidity. Alkaline bacterial fermentation of the urine outside the urinary tract is often responsible for an alkaline reaction, especially when the urine is kept in a warm place.

The following pathologic conditions either diminish the acidity of the urine or render it alkaline:

1. Abnormal conditions of gastric digestion.
2. The admixture of alkaline secretions from exudations of the urinary tract (cystitis, gonorrhea, rupture of abscess into the tract).
3. The rapid absorption of transudates or exudates, the alkaline salts of which are excreted in the urine.
4. The alkaline fermentation of the urine within the urinary tract.

To understand the significance of an alkaline reaction of the urine it is important to determine whether this depends upon free ammonia or upon a fixed alkali. If red litmus paper placed near the surface of the

urine is turned blue without being immersed, or if, when a glass rod dipped in dilute hydrochloric acid is held over the surface of the urine, white fumes of ammonium chlorid are produced, or if we note a strong ammoniacal odor, the reaction is caused by a volatile alkali, probably ammonia. Moistened red litmus-paper suspended for a sufficiently long time, one-quarter to one-half hour, over a normal acid urine will become blue, showing that a certain amount of ammonia, even without any apparent fermentation, is given off by a freshly voided acid urine; but this blue color will disappear when the paper is dried. It is characteristic of urines which owe their alkalinity to fixed alkalis that only upon the immersion of red litmus-paper in the urine will the paper become blue, and that this color is permanent even upon the application of heat.

Whenever the reaction of the urine is alkaline from free ammonia, it is safe to assume that the condition is the result of the decomposition of the urine or ammoniacal fermentation. To decide whether this has taken place within or outside the urinary tract, it is necessary to test the urine directly after it has been voided.[1]

The alkaline fermentation of the urine brought about by the action of micro-organisms is characterized by the change of urea, $CO<\begin{matrix}NH_2\\NH_2\end{matrix}$, into ammonium carbamate, NH_2, $COONH_4$, and ammonium carbonate $(NH_4)_2\,CO_3$, with the taking on of one or two molecules of water, as the case may be. These two substances, being unstable, easily break down and give off ammonia. The alkaline reaction due to fixed alkalis is never caused by decomposition of the urine. but by other conditions already mentioned.

The urine of dogs has been rendered alkaline (without the aid of bacteria) by administering an excessive amount of milk of lime, ammonium carbamate being excreted.

The normal acidity of the urine may be pathologically increased by an increased decomposition of the body proteins, especially in fever. The cause of the acid in this case is the same as in the ingestion of food rich in protein.

It is not yet definitely determined whether patients with the so-called uric-acid diathesis excrete an abnormally acid urine. (See p. 541 et seq. for the Quantitative Estimation of the Reaction of the Urine; Acidimetry; Alkalimetry.)

SEPARATION OF THE URINES OF THE TWO KIDNEYS

Modern renal surgery frequently demands the separate examination of the urine from each kidney. This requirement is most exactly met by ureteral catheterization by means of the cystoscope, for the details of which the reader is referred to the text-books of cystoscopy.

This method requires special technical training, and may be replaced to a certain extent by the use of the so-called urinary separators, which have recently been devised. All these instruments depend upon a similar principle: the bladder is emptied, a sagittal septum is introduced into the viscus, and the separate urines are withdrawn by catheters appropriately attached to the sagittal septum.

One of the favorite instruments of this type is that of Luys (Fig. 234), which Garré [2] describes as follows:

[1] When it is not possible to examine the urine perfectly fresh, the addition of about one-third its volume of chloroform water (1 : 200), or of a few pieces of coarsely granulated camphor or thymol crystals, will preserve the specimen.

[2] Therap. Monats., 1903, No. 1.

"It consists of two metallic grooves which may be united to form a catheter of about the caliber of No. 22 (French), and having the usual curve. Since these lateral metallic grooves embrace a third flat piece, they form a two-way catheter, each side of which possesses two eyes at one extremity and a lateral discharge tube at the other. The middle piece is inclosed in a condom, which may be made tense by a screw, so that it fills the concavity of the curve. The instrument is introduced closed, the urine in the bladder is drawn, the septum is made tense by turning the screw, and, since the bladder is divided sagittally into halves, the urine from each kidney may be obtained separately. Handy accessory appliances make it possible to attach separate vessels to receive the urines from the discharge tubes. The instrument may be employed in the female with extraordinary ease, and its use in the male is not attended with great difficulty or much annoyance to the patient. In male subjects with enlarged prostates a space may be left between the gland and the catheter, which is not drained upon the introduction of the instrument, and this mixed urine may consequently interfere with the accuracy of the method. This source of error may be avoided by introducing the finger into the rectum and pressing the base of the bladder against the catheter. When the screw is reversed, the tension chain and the condom are accommodated between the grooved halves, and the instrument may be easily withdrawn. The apparatus works best with the patient in a sitting or a semirecumbent position."

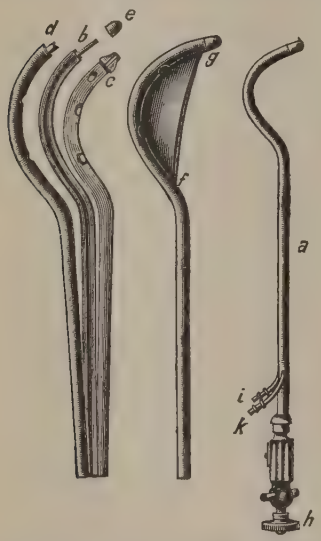


Fig. 234.—*a*, The composite instrument ready for introduction; *i*, and *k*, discharge tubes; *h*, screw to regulate the tension of the membrane; *b*, flat middle piece; *c* and *d*, grooved lateral portions; *e*, tip uniting the parts; *g f*, rubber membrane, tense. The chain is not visible in the figure.

[Cathelin's instrument has been more reliable in my hands. The sound is, however, larger, and hence more difficult to insert through a narrow meatus. Many of its best features are present in the two instruments about to be described.—Ed.]

The author has laterally employed the Lambotte separator; he considers that it presents several advantages over Luys' instrument, described above, and, therefore, he highly recommends it. The instrument is shaped like a coudé male catheter, which facilitates introduction; while the shape of the Luys' separator curve makes it difficult to introduce in the male. The instrument is lighter and cheaper, and the gutta-percha membrane unfolds more easily than in the Luys instrument. The principle is the same except that the membrane in the Luys instrument is stretched by means of a chain and protrudes from the concavity of the sound (Fig. 234), while in Lambotte's improvement the membrane is pushed out of the convex end of the sound by means of an arched watch-spring controlled by a shifting mechanism. The accompanying cut (Fig. 235) shows the instrument as it appears in the bladder with its separating membrane stretched. *a b* is the curve of the catheter, *a c e d b*, the stretched separating gutta-percha membrane. The shaft *b k* has two parallel bores, through each of which a very small soft-rubber catheter can be introduced. *e* is the inner extremity of the catheter for the right side of the bladder. It has a lateral opening; while the corresponding extremity of the left catheter is hidden from view by the dividing membrane. The opposite extremities of each catheter *f* and *g* open (see cut) into two centrifuge tubes which are attached to the shaft by a suitable framework and which serve to collect the urines from the two sides. The mechanism which stretches the membrane is not seen in the figure, being hidden by the membrane itself. It is shaped like a finger-cot, closed at *a*, open at *b*, covering the tip of the instrument from *a* to *b*, and firmly fastened at these points by threads. During the insertion of the instrument this finger-cot lies in folds along the beak, and being thin, offers no greater difficulty to the introduction than an ordinary catheter. In the original Lambotte separator, the membrane is stretched by shifting *i* upon *h*, thus shortening the beak *ab*—like the piston and cylinder of a

syringe. This moves the tip *a* in the direction of the arrow *A* and the watch-spring bends down and stretches the membrane into the position shown in the cut (*a c e d b*). The spring and membrane are retained in place by the tiny screw *k*. With this instrument no especial practice is required for the separation of the urine.

The author has found but one objection to the instrument. The beak *a b* is evidently considerably longer at the moment of introduction than later, when the membrane is stretched as in the cut. Consequently, it occurred to the author that if the instrument be introduced as far as possible into the small shrunken bladder of a woman with urogenital tuberculosis it would not reach into the bladder as far as the point *b*, but part of it would remain within the urethra and so be very apt to lacerate the latter as the membrane was stretched. To obviate this disadvantage the author has simplified the instrument by altering the mechanism for stretching the membrane. The beak *a b* is made immovable, and the spring is bowed and forced out of the shaft *k b* to the position *a c e d b* by pushing *i* in the direction of the arrow *B*. This motion is made possible by a hinge fastening the spring to the end of the sound at *a*, and another hinge at *b*, fastening it to a sliding metal rod inside the shaft, a similar principle to that of the diverticulum sound. (See Fig. 331, p. 882.) With the index-finger in the ring *h* and the thumb pushing *i* in the direction of the arrow *B*, the spring bows forward and downward, stretching the membrane into its proper position in

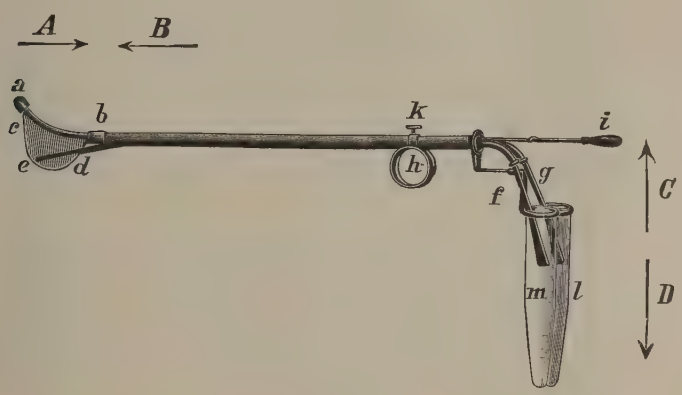


Fig. 235.

the bladder. By tightening the screw *k* this position can be maintained. Fig. 236 answers equally well for Lambotte's and the author's instrument.

The author has convinced himself, through experiments on cadavers, that the dimensions of the Lambotte model which he has followed in his own instrument assure a perfect separation both in males and females. The size of the separating membrane seems ridiculously small when compared with that of the Luys separator. It is, however, quite large enough, and the pronounced curve of the Luys model rendering introduction difficult is superfluous, provided the patient is placed so that the trigonum forms the deepest portion of the bladder (the dorsal elevated gynecologic posture), as the orifices of the ureter are only about 3 cm. from the internal orifices of the urethra. The two catheters must be introduced far enough into the bladder to reach the deepest point of concavity of the membrane, as shown in the cut. This can be determined before introduction and appropriate marks made at the ends *f* and *g*. Before introducing the sound, they must, of course, be withdrawn into the shaft.

Before inserting the instrument the bladder should be thoroughly washed as for cystoscopy, with a 4 per cent. solution of boric acid, and about 50 to 100 cc. of the liquid should be left in the bladder. After the introduction of the sound, the remaining solution flows out, filling the catheters, which then act as siphons, and the separated urine from the trigonum trickles drop by drop into the centrifuging tubes. Until the examiner becomes expert he may verify the position of the membrane by

palpating it through the vagina in a female and the rectum in a male. Light pressure is permissible, but hardly necessary once the instrument is in position, because the elasticity of the spring insures a good position. This elasticity of the spring and the membrane is a distinct advantage over the rigid curve of the Luys instrument. The separation of urine by means of this type of instrument will, in the author's opinion, replace, to a great extent, catheterization of the ureters in practice, on account of the ease with which it can be employed, and also on account of its harmlessness. The author has noted a special advantage of the spring contraction in both these models while testing the instrument in the open bladder of a cadaver, in that the separating membrane is so pliable that it can adapt itself to the most diverse forms of the neck of the bladder. The bulging of a hypertrophied prostate instead of the flat, trough-like floor of the bladder made, as is well known, the use of the Luys instrument difficult and unsatisfactory, because its flat curve could not be expected to correspond. The spring in Lambotte's or the author's model (as the author has proved upon the cadaver) may be bent to conform to such an abnormal contour. The author, however, calls attention to the unreliability of attempting such adaptation based upon rectal or vaginal palpation. One might suppose, for instance, that in cases where, owing to hypertrophy of the prostate, the floor of the bladder suddenly descends from the uretheral orifice, one should draw the separating membrane *a c e d b* more toward the urethra to insure perfect closure at *b d;* and that when the floor of the bladder is flat, one should press the instrument more toward *c*. But exactly the opposite is the correct procedure. Pressure against the spring at *d* flattens it there and curves it more sharply at *c*, while pressure at *c* makes *b d* bend to a curve, or become more nearly perpendicular. By experimenting with the instrument one can easily convince one's self of these facts. Hence, in hypertrophy of the prostate, separation will be accomplished best by rotating the shaft of the instrument in the direction of the arrow *C* on an axis about the center of the membrane; if the floor of the bladder is flat, however, the shaft should be rotated slightly in the direction of the lower arrow, *D*.

The instrument is so light and simply constructed that it is comparatively inexpensive.[1] Being so light it can be held in the hand during the collection without the aid of a stand, by resting the ulnar edge of the hand against the symphysis pubis.

Opinions differ as to the reliability of the urinary separation. Practice possibly plays a large rôle. The results are certain, however, when one discharge tube furnishes an entirely normal, and the other a pathologic, urine. If, on the contrary, both urines are abnormal, the possibility of an incomplete separation must be considered and cystoscopy finally employed.

QUALITATIVE CHEMICAL EXAMINATION OF THE URINE

EXAMINATION FOR PATHOLOGIC CONSTITUENTS

ALBUMINURIA

The clinical expression *albuminuria* applies merely to urines which contain albumin or globulin (coagulable proteins), and does not include nucleo-albumin, proteoses, nor peptone.[2]

Albuminuria may be subdivided under two heads: (1) The *true* or *renal albuminuria,* in which the albumin is excreted by the kidneys themselves; and (2) *false* or *accidental albuminuria,* in which the albumin comes from the admixture of some albuminous exudate, blood, or lymph with the urine in its course through the urinary tract. To dis-

[1] M. Schärer, Sanitätsgeschäft, A.-G., in Bern manufactures both models.

[2] It is customary to designate as albumin any protein-like substance which appears in the urine and which responds to the ordinary "tests for albumin." On this account the term albumin, although it signifies a definite class of proteins, has become synonymous with proteins, and the word is so employed in the text. As is well known, however, the proteins in the urine may consist of globulins, proteoses, etc., to the exclusion of albumins. For further characterization of these protein bodies see Cohnheim (Chemie der Eiweisskörper) and Text-book of Physiologic Chemistry, Hammarsten, translated by Mandel.

tinguish between these two forms, it is necessary to examine the urinary sediment under the microscope and to consider carefully the entire clinical picture.

Renal albuminuria is either dependent on the fact that the renal epithelium and probably principally the glomerular epithelium, is permeable to the proteins (serum-albumin and serum-globulin) which circulate with the blood, or that lacunæ are formed between individual epithelial cells, so that the tissue lymph produced in the vessel-walls is not kept back by a continuous epithelial layer. The vessels themselves cannot be responsible, because physiologically they permit the transudation of albuminous liquid in the formation of lymph. The abnormal permeability must, therefore, exist in the epithelial layers. The question of a hematogenous albuminuria in the sense of the excretion of an abnormal protein circulating in the blood seems doubtful. The only argument for this assumption is the functional albuminuria following the ingestion of large quantities of protein food. This is not altogether conclusive, for one may assign this to an irritative condition of the kidney following too great demands upon its excretory power in eliminating urea. This idea has a more reasonable basis from the finding that, after the excessive ingestion of uncooked egg-albumen, the protein excreted in the urine gives the reaction for egg-albumen itself. (See, however, p. 562.) Whether the passage of the protein through the renal epithelium is always pathologic, or, in other words, whether a so-called physiologic albuminuria can actually exist, has created considerable discussion, and some misunderstanding of terms has complicated the question. Albuminuria is usually considered the most important symptom of the diffuse kidney disorders called Bright's disease. Hence the term "physiologic" has been applied to cases of transitory albuminuria which are associated with no other symptoms, and whose subsequent development proves the absence of any real nephritis or other disturbances. Examples of this form are the albuminuria observed in apparently healthy individuals, and the so-called "cyclic albuminuria," found at certain hours of the day (generally after rising), especially in the young. As a matter of fact, the term "physiologic" means merely that this type of albuminuria is not at all serious, but it is hardly an appropriate term. Just because a biologic phenomenon is harmless, it is not necessarily physiologic. It seems to the author that we are quite as justified in designating as physiologic a catarrhal process which causes an individual no discomfort, as we are in assuming such an excretion of albumin to be physiologic. It is not physiologic, but rather due to some slight affection of the renal epithelium which causes a harmless albuminuria in otherwise healthy people, unassociated with any grave anatomic renal change.[1] This conception is of considerable importance from a practical standpoint, because the kidney of an individual with physiologic albuminuria would naturally be regarded as rather sensitive or even predisposed to actual disease, and so suggest to a careful physician appropriate prophylaxis. Perhaps it holds the same relation to actual nephritis as the alimentary glycosuria bears to actual diabetes mellitus.

[1] According to recent researches, the minute traces of protein found quite commonly in the urine of healthy people are neither albumin nor globulin, but nucleo-albumin, which has certain reactions in common with the former. (See p. 571 et seq.)

Regarding this conception of normal albuminuria, to which the term "physiologic" has so often been misapplied, one must differentiate those forms which are not detected by the ordinary clinical tests, but which are revealed by more delicate ones, but which are not associated with any obvious anatomic or clinical phenomena of a nephritis. These belong most distinctly to pathologic conditions, and the question is simply whether they are associated with an anatomic or functional disturbance. The presence of morphologic elements of the kidney is not sufficient to differentiate, for in many purely functional disturbances casts may be detected. The main diagnostic point is the ascertaining whether the albuminuria follows a distinct functional change in the condition of the patient.

Of these changes, the most important is that described by von Leube, and is due to severe muscular effort. This phenomenon is exceedingly common, and the same degree of effort reacts differently with different individuals. It is also associated with other symptoms, such as the appearance of urate sediments in the urine and the onset of muscular pains. Prolonged cold baths also sometimes give rise to albuminuria. This is probably associated with a lowering of the temperature of the blood. Mental strain may cause the appearance of albumin in the urine. The characteristic of these functional disturbances is the short duration, and their dependence on the condition provoking them.

Another group of cases is that distinguished by the longer duration of the albuminuria. In this class fall the albuminurias of the new-born which occur within the first ten days, and disappear without leaving any bad effects. The cause is not known. The urine found in the bladder of still-born children often contains albumin. Little has shown that about 50 per cent. of pregnant women have albuminuria. During labor the percentage is greater, and decreases after confinement.

One of the most important groups of albuminurias is that defined by Posner as "essential." These are undoubtedly pathologic, but are simply distinguished by the appearance of albumin in the urine. Two of these forms are the albuminuria of puberty and cyclic or orthostatic albuminuria. The albuminuria of adolescence described by von Leube occurs from the fourteenth to the eighteenth years. After this time it tends to disappear. Cyclic or orthostatic albuminuria is distinguished by the influence of position on the appearance of the protein in the urine. Urine passed during the night is free, while the vertical position of the patient will cause it to reappear in the urine. Most of these cases are included in the group of adolescent albuminurias. But some persist beyond youth, and even permanently.

In most of these cases there is a decrease in the amount of water eliminated by the kidneys, and the urine is concentrated. Some cases have their onset in later life. Armstrong found cyclic albuminuria in not less than 12 to 15 per cent. of 3000 schoolchildren. These were mostly weak individuals with juvenile enlargement of the heart. Most of these disappeared about the seventeenth year without leaving any trace. All writers are not in harmony regarding the significance of these cases. According to Senator, many of these cases are to be looked upon as simple nephritis, while Krehl and Broadbent oppose this view. The author believes that they are due to functional weakness incident to imperfect development. In the urine usually only hyaline casts are found. Regarding the cyclic albuminurias the author is inclined to agree with Hooker and Erlanger that the appearance of albumin is dependent on a disturbance in the circulation. These investigators found that at the time of its appearance the difference between the maximum and minimum blood-pressure was low. Others have been able to show not only a low arterial pressure, but a low maximum arterial pressure.

Phosphatic albuminurias are also found, in which, with the phenomena of a phosphaturia, one finds traces of albumin in the urine.

Nutritive albuminurias are those following the excessive ingestion of protein. This has only been found in healthy subjects after eating much raw or insufficiently cooked egg-albumen. In nephritics uncooked white of egg often increases the amount of albumin in the urine. This corresponds with the fact that the injection of uncooked albumin into the circulation of animals causes an albuminuria, due to the injury of the parenchyma of the kidney by the foreign protein.

There are also cases of albuminuria minima, which are characterized by long duration or the appearance of albumin in the urine from time to time, and in which no enlargement of the heart or other clinical symptoms are obtainable. The few reports of these cases, with the portmortem findings, leave one in doubt as to the existence of an interstitial nephritis. Some of the cases are unquestionably negative. The occurrence of interstitial change is probable, but the prognosis is not always unfavorable. Many cases do not go on to the typical course of an interstitial nephritis. One can only differentiate these cases after long and careful observation. It would

seem that these cases are merely an accentuated physiologic or normal albumin excretion. This is in harmony with the idea that the boundary between pathologic and physiologic conditions is not by any means a sharp one.

Definite pathologic forms of albuminuria must certainly depend upon some affection of the renal epithelium, which is most pronounced in inflammatory and circulatory disturbances of the kidneys (nephritis) and in amyloid disease of the kidneys. But the renal epithelium also may be damaged sufficiently to permit the transudation of albumin in: *local or general anemia, cachexia, venous congestion, transitory renal ischemia, temporary occlusion of a ureter, prolonged retention of the urine in diseases of the bladder or of the spinal cord, the circulatory disturbances accompanying attacks of epilepsy, temporary compression of the thorax,* and *prolonged cold baths.* To the same category the so-called febrile albuminuria observed in various fevers belongs.

Nephritic albuminuria varies decidedly with the type of the disease. In acute nephritis a large amount of albumin, sometimes 2 per cent. or over (though generally not more than 1 per cent.), is excreted; in chronic nephritis the amount varies. The more the disease approaches the type of a true contracted kidney, despite the severity of the disease, the smaller is the amount of albumin excreted; and in an extremely chronic case it may even disappear temporarily.

The same variability and temporary disappearance may characterize *amyloid disease.*

The amount of protein in *passive congestion* is, in most cases, not very great. There are, however, exceptions, in which the amount is large. In these cases the amount of protein corresponds closely to the diminution in the volume of the urine resulting from the congestion; whereas in nephritis, on the contrary, the degree of albuminuria does not correspond in any well-defined way to the quantity of urine. A large amount of albumin and a relatively large volume of urine are hardly ever combined in passive congestion; but such a combination is not uncommon in nephritis, although ordinarily only in very serious conditions of disease.

Febrile albuminuria rarely occurs except in the severe infectious diseases, where the quantity of albumin may become so considerable that it is very difficult, perhaps impossible, to make a differential diagnosis between such albuminuria and actual nephritis.

DETECTION OF PROTEINS AND RELATED SUBSTANCES IN THE URINE

Recent opinions regarding the nature of the proteins and their derivatives have altered so materially that the reader is recommended to study the annexed table to comprehend the differences and mutual relationships of such of these substances as may occur in the urine. (See Table facing this page.)

Detection of the Ordinary Coagulable Proteins of the Urine (Serum-albumin; Serum-globulin)

(The albumin test in the usual sense of the word)

Heat Test for Albumin.—This test depends upon the principle that in weakly acid or neutral solutions albumin will be coagulated at the boiling-point. The coagulation temperature of the albumin occurring in the urine, and which is principally serum-albumin, lies between

56° and 81° C. The variations are dependent on the concentration of the solution with respect to proteins and salts A test-tube of urine is heated to the boiling-point, preferably only at the upper portion. If a precipitate (cloudiness) appears, it will consist either of albumin or of phosphates and carbonates, for the latter are also precipitated by heat. (See p. 674 et seq.) A distinct flaky precipitate would probably indicate albumin; but to be certain, the urine should be acidified drop by drop (dilute acetic acid 1 : 9). If the precipitate then dissolves, it was due to phosphates and carbonates. If it does not dissolve, but, on the contrary, becomes more flaky and heavier, it is albumin. The heat test will not always cause a precipitate in an albuminous urine which is alkaline or only very faintly acid. This is the reason why the acid is added drop by drop until the urine becomes distinctly acid. It is generally advisable to employ a dilute solution of acetic acid, because, although an alkaline urine may require considerable acid, too strong acid might allow a moderate amount of albumin to escape notice by being rapidly changed to the soluble acid albumin. Again, acidulating the urine too strongly before boiling may entirely prevent the precipitation of the albumin. In this way many cases of mild albuminuria may escape detection. If slight in amount, albumin often does not precipitate from the urine until after the lapse of some time. This is true in other tests as well as in the heat test.

The reason it is advisable to heat only the upper portion of the urine in the test-tube is because in this way we can differentiate a cloudiness due to albumin even when the urine, before heating, was not perfectly clear. In case of marked turbidity, however (such as would be caused by bacteria, pus, or excess of phosphates), the urine should be filtered before an exact test is attempted. If filtration does not succeed in clarifying the urine, it is advisable to add calcined magnesia and then filter again. This powder will clog the pores of the filter mechanically, and assist in removing a cloudiness, even that which is caused by bacteria. Cloudiness due to a considerable excess of urates will not complicate this test, because heating the urine dissolves the urates and clarifies the urine before the albumin is coagulated.

Another method of performing the heat test is first to acidify the urine strongly with several drops of dilute acetic acid, and then add one-sixth of its volume of concentrated salt solution (30 salt to 100 water). If much albumin is present, a precipitate will form even in the cold mixture and decidedly increase upon heating. The advantage of this method is that it shows the presence of albumoses, since the latter are precipitated in the cold mixture and dissolved by heating. If both albumin and albumoses are present, the latter will be precipitated by cooling the filtrate from the boiled specimen.

The nucleo-albumin in normal urine will be precipitated by either heat test. If abundant enough to produce a cloudiness upon boiling, it may be mistaken for true albumin. This confusion may readily be avoided by adding a few drops of concentrated acetic acid to a cold specimen of urine. If this acidulation produces a cloudiness of the same intensity in the cold as in the boiled urine, the precipitation in both is due to nucleo-albumin; but if the cloudiness is of less intensity, the precipitation must depend upon a combination of nucleo- and true albumin.

The ordinary heat test is one of the safest and most accurate methods

Characteristics and Reactions of the Proteins Coming Under Consideration in the Examination of the Urine.[1]

REAGENTS.	1. Serum-albumin (Albumin, proteins in the narrower sense).	Globulins. 2. Euglobulin, or Pseudo-globulin.	Globulins. 3. Fibrinogen is a globulin which has the peculiarity of being changed in solutions containing calcium by fibrin ferment (serum, defibrinated blood) into fibrin (coagulating "spontaneously").	4. Fibrin originates from fibrinogen by the action of fibrin ferment in solution of calcium salts.	Albumoses originate from 1, 2, 3, 4 by peptic and tryptic digestion as well as by the influence of acids and alkalies. Primary Albumoses. 5. Hetero-albumose.	Primary Albumoses. 6. Protalbumose.	7. Deutero-albumose (secondary albumose).	8. Peptone (Kühne). End product of the peptic and tryptic digestion of 1, 2, 3, and 4 (appearance in the urine through newer experimentation has become doubtful).	Compound Proteins. Extremely complicated combinations, which may be decomposed by boiling with diluted acids, or by peptic digestion into a protein and another substance (carbohydrate, pigment, nuclein). 9. Hemoglobin (Blood-pigment) breaks down by boiling with diluted acids into hematin and protein.	10. Nucleoprotein breaks down by peptic digestion into nuclein, and protein, contains phosphorus.	11. Mucin breaks down by boiling with diluted acids into reducing carbohydrate and protein.
Water.	Soluble.	Insoluble.	Insoluble.	*Insoluble.*	Insoluble.	Soluble.	*Soluble.*	Soluble.	Soluble.	*Insoluble.*	Insoluble.
Boiling.	*Coagulated* (in weak acid reaction).	*Coagulated* (in salt solutions).	*Coagulated* (in salt solution).	*Coagulated.*	*Coagulated* (in salt solutions).	*Coagulated* (in salt solutions).	*Not coagulated* (in salt solutions).	*Not coagulated.*	*Coagulated and decomposed.*	*Coagulated.*	?
Alcohol.	Precipitated and coagulated.	Precipitated and coagulated.	Precipitated and coagulated.	Insoluble.	Precipitated (out of neutral solution).	Precipitated (out of neutral solution).	Precipitated (out of neutral solution).	Precipitated.	Precipitated and coagulated.	Precipitated (partly changed).	Precipitated.
5 to 10 per cent. neutral salt solutions.	Soluble.	Soluble.	Soluble.	Insoluble.	Soluble.	Soluble.	Soluble.	Soluble.	Soluble.	?	?
Saturation of the solution with NaCl.	Not precipitated.	Incompletely precipitated.	Completely precipitated.	. . . . .	Almost completely precipitated.	Very incompletely precipitated.	Not precipitated.	Not precipitated.	Not precipitated.	?	?
Saturation of the solution with $MgSO_4$.	*Not precipitated* (thrown out of a saturated solution by acetic acid).	*Completely precipitated.*	*Completely precipitated.*	. . . . .	?	Very incompletely precipitated.	Not precipitated.	Not precipitated.	Not precipitated.	*Precipitated.*	*Not precipitated.*
Saturation of the solution with $(NH_4)_2SO_4$.	*Completely precipitated, but only with complete saturation.*	*Completely precipitated with half saturation.*	*Completely precipitated.*	. . . . .	*Completely precipitated.*	*Completely precipitated.*	*Incompletely precipitated.*[2]	*Not precipitated.*	?	?	?
Dilute alkalies.	Not precipitated; will be changed by an excess into albuminates.	Not precipitated; will be easily changed by excess into albuminates.	Not precipitated; will be easily changed by excess into albuminate.	Swells up.	Not precipitated.	Not precipitated.	Not precipitated.	Not precipitated.	Decomposed.	Partly soluble, partly swelling into slimy masses.	Soluble.
Dilute acids.	Not precipitated, and by excess gradually changed into acid albumin.	First precipitated; by excess gradually changed into acid albumin.	Not precipitated (in alkaline solution only precipitated). By excess gradually changed into acid albumin.	Greatly swollen (especially in 0.3 per cent. HCl).	Not precipitated.	Not precipitated.	Not precipitated.	Not precipitated.	Decomposed.	Easily soluble in mineral acid, very difficultly in acetic acid.	Soluble in mineral acid, not in acetic acid.
Concentrated mineral acid.	Precipitated, and by excess gradually changed into acid albumin.	Precipitated, and by excess gradually changed into acid albumin.	Precipitated, and by excess gradually changed into acid albumin.	Gradually dissolved as acid albumin.	?	?	?	Not precipitated.	Decomposed.	Soluble.	Soluble.
Metaphosphoric acid.	Precipitated.	Precipitated.	Precipitated.	. . . . .	Precipitated.	Precipitated.	Precipitated.	Not precipitated.	Decomposed.	?	?
Nitric acid.	Precipitated; precipitate insoluble upon heating.	Precipitated; precipitate insoluble upon heating.	Precipitated; precipitate insoluble upon heating.	. . .	Precipitated, soluble upon heating.	Precipitated, soluble upon heating.	Not precipitated (unless NaCl is present).	Not precipitated.	Decomposed.	Precipitated, soluble in excess.	?
Potassium ferrocyanide + acetic acid.	*Precipitated.*	*Precipitated.*	*Precipitated.*	. . . . .	*Precipitated, soluble upon heating.*	*Precipitated, soluble upon heating.*	*Precipitated, but only by strong concentration, soluble upon heating.*	*Not precipitated.*	Decomposed.	*Precipitated.*	?
Common salt + acetic acid.	Precipitated.	Precipitated.	Precipitated.	. . . . .	Cloudy upon heating.	Precipitated, soluble upon heating.	Precipitated, soluble upon heating.	Not precipitated.	Decomposed.	Incompletely precipitated.	?
Tannic acid in mineral acid solution.	Precipitated.	Precipitated.	Precipitated.	. . . . .	Precipitated.	Precipitated.	Precipitated.	Precipitated.	Decomposed.	Precipitated.	?
Trichloracetic acid.	Precipitated.	Precipitated.	Precipitated.	. . . . .	Precipitated.	Precipitated.	Precipitated.	Not precipitated.	Decomposed.	?	?
Phosphotungstic acid in mineral acid solution.	Precipitated.	Precipitated.	Precipitated.	. . . . .	Precipitated.	Precipitated.	Precipitated.	Precipitated.	Decomposed.	Precipitated.	?

[1] The statements of the synopsis refer to the pure substances, and the reactions may be modified by the presence of other substances in the urine. The expression "coagulated" is used in this synopsis in contrast to "precipitated," if the precipitate, produced by heating or by alcohol, has become insoluble in water or in neutral salt solutions. For the sake of distinction the most important reactions are printed in heavy type in this synopsis.

[2] According to Neumeister, deutero-albumose originating from protalbumose will not be completely precipitated.

of determining the presence of coagulable protein. (See below in regard to its advantages.) But we must remember that not only nucleo-albumin and albumose, but also resinous acids, may be precipitated by acidifying the urine too strongly. (See below for the Nitric Acid Test Relative to the Differentiation Between Resins and Proteins.)

Tests for Albumin in the Cold.—A large variety of chemical reagents are capable of precipitating albumin even at a low temperature. Requiring no alcohol lamp, these tests are of distinct advantage to the practitioner. The best known are:

The Nitric Acid Test (Heller's Test).—One-half inch of concentrated nitric acid is placed in a test-tube, and filtered urine is allowed to flow down the sides of the tube and stratify itself upon the acid. Albumin, if present, causes a precipitate at the line of junction of acid and urine, and forms a ring or zone of cloudiness. If, however, there is only a very small amount of albumin present, this precipitate may not separate until after the lapse of several minutes.

Under certain conditions, *e. g.*, a very concentrated urine, the uric acid or urates may be precipitated by this test; but if the zone is quite flocculent, it will probably be due to albumin. To be absolutely sure the specimen should be gently heated (not boiled), when the ring, if due to urates or uric acid, will promptly disappear. Or, before testing, the specimen can be diluted with two or three times its volume of water, in which case nitric acid will precipitate only albumin. Moreover, the uric-acid ring is usually broader, less sharply defined along its upper border, and often plainly situated in the urine itself above the line of junction of the two fluids.

After the internal administration of some of the balsams the nitric acid test sometimes brings down a precipitate of resinous acids, which may be confused with that of albumin. Such a precipitate, however, will be to some extent cleared up by heat. Or, if the nitric acid and urine are mixed and the liquid then sucked up from the precipitate with a pipet, the precipitate, if composed of resinous acids, will dissolve in an excess of alcohol. According to Tappeiner, it is sufficient to add two volumes of alcohol to the mixture of urine and nitric acid without first separating the precipitate.[1] Alexander has objected that certain proteins precipitable by nitric acid will, under certain conditions, be dissolved in alcohol as well as in resinous acids. He recommends the solution of the precipitate by the addition of ether, although a great excess of the latter will be necessary to prevent the formation of an emulsion. A precipitate soluble in ether is due only to resinous acids. The heat test also permits a differentiation, for the resinous acids are not precipitable by heat unless the urine has been very strongly acidulated with acetic acid. Alexander performs a control test by adding to the heated urine one-third its volume of nitric acid; any cloudiness must then be due to albumin, since the resinous acids could not be precipitated because of the heat and the considerable excess of nitric acid. Another characteristic of the resinous acids is that the addition of a few drops of hydrochloric acid produces a cloudiness of the urine. (See p. 612, Balsams of Copaiba and Sandalwood Oil.)

Albumoses and nucleo-albumin are also precipitated by the nitric acid test; but the latter is dissolved by an excess of acidity, and the former by heating.

[1] Deut. med. Woch., 1893, No. 14, p. 323.

Under certain conditions nitric acid precipitates the bile acids, and in very concentrated urine, the urea, as urea nitrate. To prevent this and the other sources of error mentioned above, Hammarsten suggests a dilution of the urine to a specific gravity of 1005 or lower. Heller's test then precipitates only albumin, nucleo-albumin, and albumoses, because, unless the urine is concentrated, neither uric acid, urea, the bile acids, nor the resinous acids can be precipitated. Albumose can then be excluded if the precipitate persists after warming.

Test with Acetic Acid and Potassium Ferrocyanid.—The specimen is strongly acidified with acetic acid, and a solution of potassium ferrocyanid (1 : 10) is then added drop by drop; the slightest amount of albumin will cause the appearance of a cloudiness or a precipitate. This reaction is one of the most trustworthy of all the tests for protein. Nevertheless, the albumoses and nucleo-albumin will also be precipitated (the former, however, only when present in considerable concentration).

Tanret's Test.—The reagent is prepared by dissolving 1.35 gm. of mercuric chlorid and 3.32 gm. of potassium iodid in as little water as possible and adding 50 cc. of water and 20 cc. of acetic acid. The reagent is added drop by drop to the urine, until a precipitate is produced. The reaction is an exceedingly delicate one. It reacts not only with albumin, but with albumoses, peptones, and alkaloids. It is too delicate for the detection of pathologic amounts of albumin.

Spiegler's Test.—The reagent is made by mixing together 8 gm. of mercuric chlorid, 4 gm. of tartaric acid, 20 gm. of glycerol, and 200 cc. of water. Jolles' modification of the reagent is prepared as follows: 10 gm. of mercuric chlorid, 20 gm. of succinic acid, 10 gm. of sodium chlorid, and 500 cc. of water. This reagent is probably the most delicate test for albumin which we possess. The urine is filtered and made acid with acetic acid in order to keep carbonates in solution, and also to precipitate those substances which are brought down by cold acetic acid. The urine is then filtered. It is then poured gently on top of the reagent. If albumin be present, a ring is formed at the point of junction. According to Jolles, the reagent detects albumin in a concentration of 1 : 350,000. For the detection of pathologic albuminurias the test is too delicate.

Metaphosphoric Acid Test.—If a small particle of this substance (HPO_3) is dropped into albuminous urine, the protein will be precipitated. The test is of little value, because it applies only to fairly large amounts of protein—0.1 per cent. or more. The same precautions as before must be observed in order to distinguish urates, uric acid, and resinous acids. The only advantage this test possesses is that the metaphosphoric acid can be readily transported as a solid, although it must be kept sealed to prevent the absorption of water and a resulting change to the ordinary phosphoric acid, which does not precipitate protein.

Picric Acid Test.—Picric acid, either in the solid substance or in solution, may be used like metaphosphoric acid. It precipitates albumoses, peptone, nucleo-albumin, resinous acids, and sometimes uric acid, urates, and creatinin.

Since with these cold tests so many precautions are necessary, it becomes evident that the practitioner will select the ordinary heat test for albumin (p. 563 et seq.) as being the most reliable and the simplest.

Appendix.—*To Remove Protein from the Urine.*—This is often necessary before many of the following qualitative and quantitative tests can be performed. The best method is to effect an insoluble combination with it and some metallic oxid. Hofmeister adds 10 cc. of a saturated solution of sodium acetate to half a liter of urine, and into this mixture stirs a solution of ferric chlorid, drop by drop, until the color becomes blood red. Such a mixture, which is strongly acid, is then exactly neutralized with sodium or potassium hydroxid, or at most allowed to remain very faintly acid, and then boiled, cooled, and filtered. The filtrate should be free from protein and iron. (Test with potassium ferrocyanid.) The method is of no value for a urine containing sugar, because the oxid of iron would be kept in solution.

It is usually sufficient to boil an acid urine until the protein is coagulated, and then to remove the latter by filtration. If the urine be alkaline or neutral, it should be slightly acidulated with dilute acetic acid. When the protein coagulates as a sort of cloudiness rather than in flocculi, it is advisable to add a little more acetic acid, while still boiling, until large flocks form. If coagulation by boiling does not produce coarse flocks, filtering will not completely remove the protein. If the

acid reaction be too faint, or if too much acetic acid be added, the protein may be prevented from separating in large flocks. Schorer, one of the author's assistants, has found that a solution of azolithmin gives a good indication for the optimum acidity of the urine. Enough of the indicator is added to color the urine. When sufficient acetic acid has been added, the violet tinge changes to red. If too much acetic acid has been added, the excess may be removed by the cautious addition of a weak solution of sodium carbonate. If, during heating, the red color changes to violet, a little more acid must be added to bring the reaction back to the proper point. If the amount of protein be large, it is a good plan to first dilute the urine with water before attempting to make a separation. The only way to be certain that the protein has been completely removed is to be sure that the addition of acetic acid and potassium ferrocyanid to the filtrate does not produce any cloudiness. If any turbidity still persist, it is due to the addition of too much or too little acid, and the test should be performed again, varying the acidity slightly.

Detection of Globulin

Globulin always seems to accompany serum-albumin in urine, and not to be present without it. Regarding the diagnostic significance of the globulin content of the urine see p. 616. According to more recent investigations, there are three groups of globulin—euglobulin, pseudoglobulin, and fibrinoglobulin or fibrinogen; the last is spoken of on p. 568. The globulins are insoluble in water, and are held in solution by the salts contained in the urine. To demonstrate globulin we add enough ammonia to make the urine neutral or faintly alkaline. This is done in order to precipitate the phosphates, which, in the subsequent treatment with ammonium sulphate, would produce a turbidity. Then we filter, and add to the filtrate an equal volume of saturated ammonium sulphate solution. After the resulting precipitate has settled well (one hour) it is collected upon a filter, and then washed with a half-saturated ammonium sulphate solution until the filtrate is protein-free. The precipitate contains the globulin and fibrinogen, and under certain conditions, albumoses as well. The albumin has not yet been precipitated, because this requires *complete* saturation with the reagent. (See Table facing p. 563.) The precipitate is next dissolved in a little water and the filtrate heated over a water-bath. This will coagulate the globulin, fibrinogen, and albumose. This precipitate is filtered, washed with water, and then digested and dissolved in a 1 per cent. solution of soda over a water-bath. If necessary, the resulting solution can be filtered again, and then carefully neutralized with acetic acid. If any globulin or fibrinogen was originally present, an albuminate will be precipitated which will not be dissolved by the addition of a solution of sodium chlorid. If the deposit consists of albumose, acetic acid either gives no precipitate whatever or the precipitate is dissolved by a solution of sodium chlorid. Solutions of fibrinogen differ from those containing globulins in that the latter are not coagulated by the addition of fibrin ferment (fresh blood-serum). This difference, however, is of no practical value in urinary examinations, as will be observed in the subsequent observations upon the demonstration of fibrinogen in the urine.

When large quantities of globulins are present, the urine, when dropped into distilled water, produces a turbidity. Likewise a drop of acetic acid produces a turbidity in urines containing much globulin if the urine be diluted with water to a specific gravity of 1006. Other substances are at the same time precipitated by acetic acid. (See p. 570.)

Detection of Fibrinogen

Fibrinogen belongs to the globulins, and is precipitated like serum-globulin (see above). The test for it is practically very simple, however, because fibrinogen will coagulate spontaneously in the presence of lime salts and fibrin ferment. Now when fibrinogen is present in the urine, these last two factors necessary for coagulation are never absent, so that if a coagulation occurs spontaneously when the urine is allowed to stand, the presence of fibrinogen is always indicated. This phenomenon is usually associated with a *considerable admixture of blood in the urine.* The coagulation then resembles an ordinary blood-clot. Spontaneous coagulation occurs very exceptionally in the urine without an admixture of blood. So far as we know now, this has been observed only in *tropic chyluria* and in *very rare cases of nephritis.*

Detection of Fibrin

Fibrin forms in the urine when the latter contains fibrinogen. It occurs in the form of small clots, which are easily recognized under the microscope by their shredded structure, and are oftentimes tinged with blood. These physical peculiarities and the fact that it swells in dilute acetic acid will suffice for its recognition.

DETECTION OF ALBUMOSES

(Albumosuria—Propeptonuria; Peptonuria)

The terms *albumosuria*, *propeptonuria*, and *peptonuria* should be considered synonymous and all three included in the term *albumosuria* (better proteosuria), because the term peptonuria was applied at a time when peptones and albumoses had not been differentiated, and because so-called "*true peptone,*" which has since been distinguished from the albumoses by Kühne, has not been absolutely proved to occur in the urine. (See Table facing p. 563.) Another reason why *albumosuria* and *peptonuria* should be included under one term is that Kühne's separation of *true peptone* from the albumoses is somewhat artificial and based upon one single reaction, the precipitation of the *albumoses* by ammonium sulphate and the non-precipitation of *true peptone.* Moreover, even this reaction does not permit of any sharp distinction between them, for certain of the albumoses are not completely precipitated.

The *albumoses* have been found in the urine both by themselves and combined with albumin *during the puerperium,* in *acute yellow atrophy of the liver,* in *phosphorus-poisoning,* in *ulceration of the stomach and intestines* (enterogenic albumosuria), in *most febrile conditions,* especially in the *infectious diseases,* particularly the *suppurating processes* (pyogenic albumosuria), in *pneumonia* during resolution, in *scurvy,* in *nephritis.* In enterogenous albumosuria the albumoses may be due to these proteins being absorbed from the intestine, and which have been subsequently reconstructed into albumins. In the other conditions they are probably due to autolytic processes occurring in various organs of the body.

The presence of the *albumoses* in the urine is of clinical importance only when the urine does not contain albumin, because in albuminuria the albumoses are almost always to be found in the urine after removal of the albumin. It then appears questionable whether they existed pre-

formed or were formed from the albumin by the chemical processes employed for its removal.

The presence of albumoses alone in the urine is of only limited diagnostic value. But when it is very pronounced, and when there are no other reasons for albumosuria, it may lead to the recognition of *deep-seated suppuration*. This symptom must, therefore, be considered in the *diagnosis of perityphlitis*, in the differential diagnosis between *tuberculous and purulent meningitis*, in the diagnosis of *abscess of the brain*, and of *empyema of the pleura*, etc.

Salkowski's[1] **Test for Brücke's Peptone or Albumoses.**—This is a modification of Hofmeister's early method. Fifty cubic centimeters of urine free from coagulable protein are required. If the specimen contains nucleo-albumin, the latter may be precipitated with a little neutral lead acetate. A thick flocculent precipitate appears (with which, by means of filtration, the nucleo-albumin is removed). "The filtrate is then placed in a beaker with 5 cc. of HCl, precipitated with phosphotungstic acid, and then heated over a wire gauze. In a few moments the precipitate collects in a resinous mass at the bottom of the glass. The supernatant fluid is then decanted as completely as possible, and the resinous mass is washed twice with distilled water, which, if done carefully, may be accomplished with scarcely any loss. We now add to the precipitate about 8 cc. of water and 0.5 cc. of sodium hydroxid (of about 1.16 specific gravity). The precipitate now crumbles and easily dissolves when the beaker is gently shaken. The resulting solution, usually of a deep-blue color, is heated again over the wire gauze. It usually becomes turbid and dirty-grayish yellow; sometimes it turns yellow but remains clear. If the discoloration occurs slowly, it may be hastened somewhat by the addition of a few drops of sodium hydroxid. When it is completed, the liquid is poured into a test-tube, cooled, and the biuret reaction[2] tried. For this purpose a dilute (1 to 2 per cent.) solution of copper sulphate is added drop by drop with shaking. If peptone is present, the liquid will turn a decided red, and this color will be intensified if the liquid is now filtered. The whole process does not occupy more than five minutes. Another great advantage of the method lies in the fact that, owing to the small amount of urine required, nucleo-albumin is less liable to affect the reaction."

The addition of a few drops of barium chlorid solution has seemed to the author distinctly advantageous when the solution upon which the biuret reaction is to be performed is already colored. After filtering off the resulting precipitate, the solution will be decolorized.

Salkowski has discovered a source of error in his own method which decidedly interfered with its practicability.[3] He found that the albumose reaction might be simulated if the urine contained much urobilin, for with the biuret test urobilin gives a color very much like that obtained with the albumoses. To make the value of a positive biuret test absolute, Salkowski therefore considers that the solution must first be shown to furnish no spectroscopic evidence of urobilin (p. 584). If the urine contains much urobilin besides albumoses, we should first extract with amyl-alcohol after acidifying, in order to remove the urobilin as completely as possible. By this plan, however, some loss of albumose can hardly be prevented. Employing barium chlorid, as suggested above, will sometimes, but not always, free the urine from urobilin.

v. Aldor[4] modified Salkowski's test in order to eliminate the urobilin. He separates the phosphotungstic acid precipitate by centrifugalization instead of by heating the fluid, then washes repeatedly with alcohol, which takes up the urobilin, and centrifugalizes again until it becomes absolutely colorless. The washed precipitate is then suspended in water and dissolved in sodium hydroxid, and finally

[1] Centralbl. f. d. med. Wiss., 1894, xxxii, 113, and Praktcum der physiol. Chemie, second ed., 1900.

[2] The *biuret reaction* is a color reaction common to all proteins in solution. It is, however, especially marked with albumoses and peptones. It is performed as follows: After an excess of sodium or potassium hydroxid has been added to the solution of protein a very dilute copper sulphate solution is added. It will produce a violet color, the shade varying according to the kind of protein present; with albumins it is a blue violet; with peptones and albumoses it is a red violet.

[3] Berlin. klin. Woch., 1897, No. 17, p. 353.

[4] Ibid., 1899, Nos. 35 and 36.

the biuret test is performed. If no centrifuge is available, the precipitate may be washed on filter-paper with alcohol.

Detection of Albumoses According to Schultess'[1] Method.—The urine is first filtered, and any nucleo-albumin which may be present is precipitated by dilute acetic acid and removed by filtration. Then the tests for coagulable protein are made—the heat test, ferrocyanid test, and Heller's test. Urine containing coagulable protein need not be examined further, because it is of no clinical interest. (See p. 568). If this is absent, 20 to 30 cc., prepared as above, are dropped into six times the quantity of absolute alcohol and then allowed to stand for twelve to twenty-four hours. The solution is then decanted and the precipitate dissolved in a slight amount of warm water. After refiltering and testing the solution again for precipitable nucleo-albumin with very much diluted acetic acid, the biuret reaction is performed. The presence of urobilin in the urine (see Salkowski's method) does not, as a rule, give rise to any difficulty in this case, because when precipitation is accomplished, the urobilin remains in solution. In any case the precipitate may be washed with absolute alcohol, and so completely freed from urobilin.

Detection of the Bence-Jones Substance (Formerly Called Heteroalbumosuria, Kahler's Disease (Multiple Myeloma), Bradshaw's Albumosuria.—The Bence-Jones substance is a peculiar one and is found infrequently in the urine. It is characterized by certain properties which led the author in previous editions of the book to classify it with the primary albumoses. The more recent investigations of Magnus-Levy[2] and Lindemann have shown that it must be separated from the group of albumoses, and be placed in that of the native proteins. The Bence-Jones substance was at first found only in cases of multiple myelomata (Kahler's disease). Askanazy has, however, shown[3] that its appearance is not pathognomonic for this condition, as he has also found it in a case of lymphatic leukemia. In all other cases, however, it occurred in widely diffused, advanced tumors of the bone-marrow, soon ending fatally. The amount of the substance which may be found in the urine is very considerable, varying from 1 to 7 per cent. Occasionally the excretion ceases for a time. The substance is found in the blood, bone-marrow, and the hydropic fluid of patients suffering from the disease. In one case it was absent from the urine, but was found in the pleural fluid. Occasionally the urine is turbid when passed, due to the partial precipitation of the substance. The amount eliminated is independent of the diet.

Detection of the Bence-Jones Substance.—According to Spaeth, a urine which contains the substance is characterized by the following test. The urine is made acid with acetic acid, and if it contains enough sodium chlorid, will become turbid when heated to 50°, and at 60° C. deposits a non-flocculent gummy precipitate which adheres to the sides of the vessel. Part of the precipitate rises to the surface. By further heating, the precipitate dissolves completely, leaving the fluid perfectly clear. On cooling, it is reprecipitated. Microscopically, the precipitate consists of aggregates without crystalline structure. On account of its peculiar behavior on heating, Hougounenc describes the appearance of the substance as a thermolytic albuminuria. On account of its solubility, it has been classed with the albumoses. With regard to its precise classification the reader is referred to the original papers.

The solubility of the precipitate on heating is also shown in the nitric-acid test, and on that with potassium ferrocyanid and acetic acid. A precipitate is formed in these tests which is like that of an ordinary albuminuria. It, however, dissolves on heating. In the sodium chlorid heat test described on p. 564 a precipitate is formed in the cold, and dissolves on warming. When the solution cools, the precipitate reappears. This peculiarity will direct the attention of the clinician to the presence of the Bence-Jones substance.

Detection and Character of the Mucin-like Substances Precipitated by Acetic Acid in the Cold (Mucin, Nucleoalbumin, Euglobulin, Mörner's Protein, Nucleohiston)

Under physiologic and pathologic conditions a small amount of acetic acid when added to the urine produces, at the most, a very

[1] Deut. Arch. f. klin. Med., 1897.

[2] Magnus-Levy, Zeit. physiol. Chem., xxx, 239. The literature is given here. Matthes, Cong. f. inn. Med., 1896. The distinction made is between the true albumoses and the Bence-Jones substance. Rosin, Berlin. klin. Woch., 1897, No. 48, p. 1044.

[3] Deut. Arch. f. klin. Med., lxviii, Nos. 1 and 2, p. 34.

slight precipitate. At one time it was customary to assume that the substance was mucin. More recent investigations have shown that the substance is not a true mucin, but belongs to the group of nucleo-albumins. The two classes of substances are difficult to differentiate by a simple reaction. Physically, they are much alike. Chemically, they show important differences. Mucin is a glucoprotein, nucleo-albumin, a phosphoprotein. The mucins do not contain phosphorus, and yield on hydrolysis a protein and a carbohydrate. The nucleo-proteins contain phosphorus, and give a substance containing phosphorus (nuclein) and a protein. Mörner's[1] investigations have still further complicated the matter. He has shown that the greater number of the precipitates which are thrown down by acetic acid are due to a compound of serum-albumin with chondroitin-sulphuric acid, which decreases the solubility of the albumin. According to the relative proportions of the albumin or the paired sulphuric acid, the precipitate which is formed on the addition of acetic acid has the characters of serum-albumin or nucleo-albumin.

Later Stähelin[2] grouped some of the precipitates in the class of globulins. This observation was confirmed by Rostoski (Sitzungsberichte der med. Ges. Würzburg). Matsumuto found the precipitate to consist of fibrinogen and euglobulin. Oswald (Zeit. ges. Biochemie, 1904, v) found the same substances.

As is seen, a number of substances have been found in the precipitate produced by acetic acid, and for each of them trustworthy observations are responsible. It is therefore advisable, as the differentiation is a difficult one, to group them simply in the class of substances precipitated by acetic acid.

Mörner suggests the following differentiation (excluding the globulins which were not considered in his investigation). The salts are removed from a large quantity of the urine by dialysis. To every liter, 2 cc. of acetic acid are added. The precipitate is dissolved in a little water, and reprecipitated by acetic acid. It is then digested for some time with 5 per cent. hydrochloric acid on a water-bath. If both sulphuric acid and a reducing substance can be detected in the liquid, Mörner suspects the compound of chondroitin-sulphuric acid with protein. If no sulphuric acid can be detested, a true mucin is present. If both sulphuric acid and a reducing substance be absent, and the substance yields phosphoric acid and nuclein bases after digestion with pepsin-hydrochloric acid, a nucleo-albumin is present. These tests are not within the range of ordinary clinical methods.

Lilienfeld's nucleohiston may be also precipitated by acetic acid. This substance contains phosphorus. It has been found in the urine as a result of the breaking down of leukocytes in cases of leukemia. Its identification may be made by the method of Kolisch and Burian.[3]

Mucin is found in the urine partly dissolved, but the greater part is not in solution. The undissolved part forms the physiologic nubecula of the urine, which is seen in the urine after it has stood some time. It floats in the urine, and forms a cloud. Pathologically, it is seen in increased amount in cystitis and pyelitis, and forms the so-called mucin sediment. With an increase of mucin, there is usually an increase in nucleoalbumin, resulting from the breaking down of epithelium. This increases the difficulty of differentiation.

The general detection of these substances may be made with an

[1] Skand. Arch. Physiol., 1895, vi, 332.
[2] Münch. med. Woch., 1902, p. 1413.
[3] Zeit. f. klin. Med., 1896, xx, 374.

excess of concentrated acetic acid. If a precipitate is formed after the urine has been diluted, the presence of these substances may be suspected. The urine is diluted to prevent the salts of the urine dissolving the precipitate, and also to keep the urates in solution. The globulins are also precipitated from dilute solutions by acetic acid, but are soluble in excess. Uric acid and resin acids are precipitated by acetic acid. As these may be confused with the mucin substances, a control test should be made with hydrochloric acid. With this reagent, the uric acid and resin acids will be precipitated; the mucin substances will remain in solution.

All the usual tests for proteins, the heat test, nitric-acid test will react with mucins, nucleoalbumins, Mörner's compound, and globulins.

Detection of Hemoglobin (Blood Coloring-matter) and its Nearest Derivatives: Hematuria; Hemoglobinuria

Blood coloring-matter as it appears in the urine may arise from the admixture of blood in the kidneys or in the urinary passages, or from the transudation of dissolved hemoglobin from within the vessels. In the first case we speak of *hematuria;* in the second, of *hemoglobinuria. Hematuria* is found in all kinds of inflammation of the kidneys or of the urinary tract, in new-growths which involve any portion of these organs, in varices, aneurysms, and in tuberculosis, in renal or bladder calculi, and after traumas which bruise, injure, or tear the kidneys or urinary tract.

Besides this, one must mention the so-called renal hemophilia. The condition described by Senator is without doubt a distinct one, but many of the cases which have been described under this name are undoubtedly revealed as chronic nephritis on microscopic examination. In women the genitals should be considered in any case of admixture of blood. *Hemoglobinuria* accompanies certain toxic conditions, such as poisoning with potassium chlorate, with truffles, arsin, hydrogen sulphid, pyrogallic acid, etc. To this group also belongs the hemoglobinuria of black-water fever in cases of malaria which have been treated with excessive doses of quinin and which have become hypersensitive to the drug. Hemoglobinuria has also been observed after transfusion of blood of another species, and also in transfusion of blood from man to man, after severe burns, in severe infectious processes (seldom), and finally as an independent disease, the so-called periodic hemoglobinuria described by Lichtheim and Ehrlich. A review of this condition and more recent investigations are given by Stempel,[1] and also by Donath[2] and Choroschilow.[3] Hemoglobin can often be recognized in the urine by its characteristic color. (See p. 554.) In *hematuria* the blood-corpuscles always make the urine turbid, whereas in *hemoglobinuria* the urine may be perfectly clear. The urine may, however, be turbid in hemoglobinuria, because it may contain casts (see p. 688) and granular masses of hemoglobin (see p. 679), and because, too, hemoglobinuria is usually combined secondarily with nephritic processes (casts, renal cells, red and white corpuscles). Nevertheless, in such cases, if the urine be allowed to settle, the clear, supernatant fluid will

[1] Centralbl. f. d. Grenzgebiete der Med. u. Chir., 1902, vol. v.
[2] Zeit. klin. Med., lii.
[3] Zeit. f. klin. Med., 1907, vol. lxiv.

still exhibit a bloody color. Of course, we must remember that after a hematuria urine has stood for some time many of the blood-corpuscles will dissolve. Hence, we need as fresh a specimen as possible to distinguish between hematuria and hemoglobinuria.

If the urine remain in the bladder for a long time, the hemoglobin changes to methemoglobin. This is especially the case in slow bleeding from a kidney affected with parenchymatous nephritis, such as is seen in cases of chronic hemorrhagic nephritis. In these cases the urine is more brown or black in color than red.

The presence of red corpuscles can be demonstrated under the microscope. (Compare Organized Admixtures and Sediments of Urine.) Hemoglobin itself, whether dissolved or still contained in the red corpuscles, can be shown to be present in the urine by the following means:

Chemical Detection of Hemoglobin.—The different derivatives of hemoglobin which are found in the urine react alike to the chemical tests. (Compare Spectroscopic Test, p. 574.)

Heat Test.—In performing the heat test for coagulable protein (p. 563 et seq.), if hemoglobin be present, a brownish coagulum will result. This test is not very delicate. In contradistinction to the protein precipitate, the coagulum tends to float upon the surface of the fluid. Shaking with alcohol and sulphuric acid will bleach the color.

Heller's Blood-test.—To a test-tube half full of urine 5 drops of potassium or sodium hydroxid are added and the mixture heated. If hemoglobin be present, a brownish-red or blood-red, flocky precipitate appears. It consists of the phosphates and carbonates of the earthy alkalis which have carried down with them the hematin that has been formed from the hemoglobin in the reaction. In alkaline urines the above method often produces no precipitate, because the phosphates and carbonates have already completely separated out spontaneously. The necessary quantity of phosphates and carbonates may be supplied by adding to the specimen about the same volume of a normal urine. With this test the coloring-matters which appear in the urine after the use of chrysarobin, senna, rheum, or rhamnus may react very much like hemoglobin, and so may lead to confusion. But in the latter case the red color which arises in the fluid portion of the specimen upon the addition of an alkali after cooling, and the decoloration upon the addition of acetic acid, are characteristic. (See p. 612.)

The test is very delicate. If the urine be dark, or be from a case of jaundice, so that the characteristic color may be missed, the precipitate may be filtered off. It is then dissolved in acetic acid with a characteristic red color, which appears dichroic in reflected light, and gives the absorption spectrum for hematin. Both the precipitate or the solution may be used for Teichmann's test (see below).

Hematoporphyrin also gives a red precipitate with Heller's test. The acetic acid solution does not give spectrum of hematin, but of hematoporphyrin. (See Fig. 233, p. 545.)

Teichmann's Hemin Test.—After filtration, the precipitate from the heat or Heller's test or, better still, the precipitate produced by a solution of tannic acid, is washed and dried in the air. Any hemoglobin present will be contained in this dried precipitate, which we employ for Teichmann's delicate test. A small bit of the dry material is placed upon a glass slide with a particle of sodium chlorid, a drop of glacial acetic acid is added, a cover-slip is laid upon the mixture, and the whole is heated to the steaming-point (but not to the boiling-point) for about

one minute. A little acetic acid is added from time to time to make up for evaporation. If the fluid turns brown, it is warmed gently and then allowed to evaporate. Teichmann's characteristic hemin crystals (Plate 3) are then evident on microscopic examination. Chemically, they consist of the hydrochlorid of hematin.

The test frequently fails because excessive heat is employed and the mixture evaporated too quickly, so that, of course, the characteristic crystals are not formed so readily. Very beautiful crystals are sometimes obtained when the test is performed in the cold.

Schönbein-Almén's Turpentine-Guaiac Test.—This is one of the most delicate of the blood-tests. A layer consisting of a mixture of equal parts of tincture of guaiac[1] and oil of turpentine is carefully stratified upon the top of the urine. If hemoglobin be present, a cloudy ring slowly forms at the junction of the two layers, gradually becoming an intense blue. This test will sometimes give a positive result when the spectroscopic test fails. The oil of turpentine employed must be ozonized, *i. e.*, must be old. It may be well to test the reagent first with a well-diluted blood solution. Before performing the test, we should see that the urine is acid (adding acetic acid to an alkaline urine, if necessary).

Pus in the urine may turn the reagent blue, but it is claimed that this blue color appears quite as well without the oil of turpentine (Tappeiner). This is due to the oxydase content of the leukocytes. The same modification which we mentioned upon p. 544 (shaking with ether) for examining the gastric juice may be employed with the urine to avoid the above confusion.

The Aloin and Benzidin Tests.—See Examination of the Feces, p. 546.

Spectroscopic Detection of Hemoglobin.—In employing the spectroscopic test, it does not make any difference whether the hemoglobin is still contained in the blood-corpuscles or whether it is in solution in the urine. In the urine hemoglobin usually occurs in one of three modifications—in the form of oxyhemoglobin, reduced hemoglobin, or methemoglobin. The spectra of these substances differ; they are presented in Fig. 233.

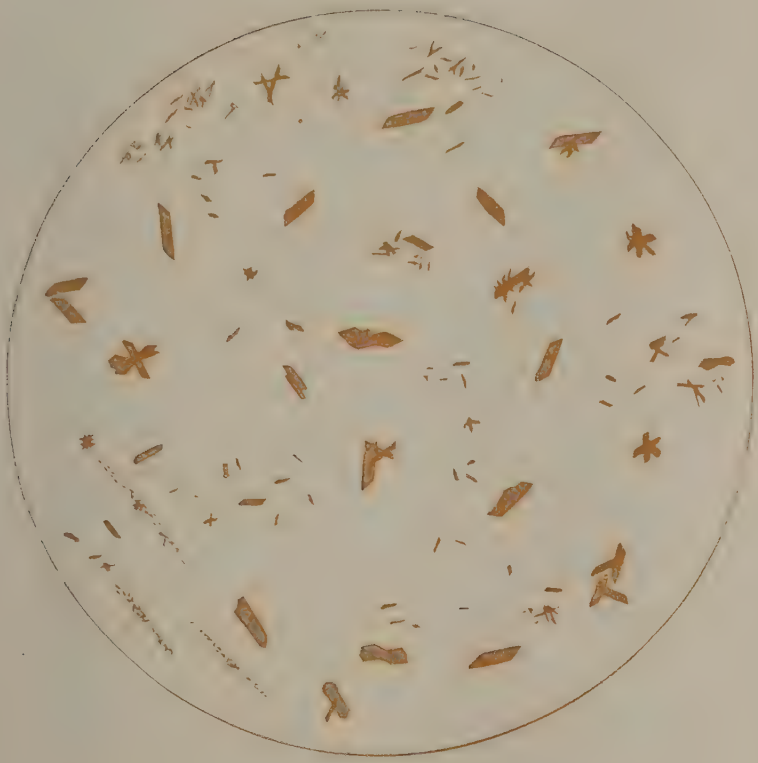
These various derivatives of hemoglobin may occur in the urine simultaneously and so produce a mixed spectrum. With a recent and profuse hemorrhage into the urinary passages we find chiefly oxyhemoglobin. With hemoglobinuria and with true nephritic hemorrhages, on the other hand, we find principally methemoglobin. The latter, however, may be altered to reduced hemoglobin, and eventually to oxyhemoglobin by bacterial decomposition.

For clinical purposes the spectroscopic test can be performed by looking at a layer of urine 1 or 2 cc. thick by transmitted bright daylight, sunlight, or lamplight, through a small hand spectroscope. (See Fig. 232.) If the urine be very dark or cloudy, it must first be diluted with water.

When the urine contains very small amounts of blood-pigment, the acetic acid solution of the hematin-containing precipitate obtained in Heller's test (see p. 573) can be used for spectroscopic examination. The hematin bands will be seen. This method may also be used when the urine is so deeply colored from the presence of bile-pigments or urobilin that the hemoglobin or methemoglobin bands cannot be seen.

[1] Alcoholic solution of guaiac resin, 1 : 5. The solution should not be old, and is best used freshly prepared. The ordinary tincture of guaiac cannot be used, as this is not prepared from the resin, but from the wood. In preparing the alcoholic solution of the resin, the green coating of the piece of resin should be removed.

PLATE 3.



Teichmann's Hemin Crystals.

DETECTION OF HEMATOPORPHYRIN

Hematoporphyrin occurs in the urine principally after the protracted administration of sulphonal, trional, and tetronal. It is also encountered in tuberculosis and other infectious diseases, pneumonia, inflammatory rheumatism, pericarditis, Addison's disease, paroxysmal hemoglobinuria, hepatic cirrhosis, hematemesis, and lead-poisoning. It also occurs rarely under pathologic conditions about which little is known.[1] Pal[2] describes a case of paroxysmal hematoporphyrinuria: only when the excretion of the substance is very pronounced does the urine show the characteristic port-wine color.

It is considered to be a red pigment derived from hematin but free from iron. Nencki and Sieber consider that it is isomeric with the biliary pigment bilirubin.

It is demonstrated by Salkowski[3] as follows: 30 to 50 cc. of urine are completely precipitated by an alkaline barium chlorid solution (a mixture of equal parts of a cold saturated solution of barium hydrate and a 10 per cent. solution of barium chlorid). The precipitate is washed with water and then with absolute alcohol, and the hematoporphyrin extracted by treating it with alcohol acidulated with hydrochloric acid.

The extraction is best performed by repeatedly pouring a warm mixture of 10 cc. of alcohol and 6 to 8 drops of hydrochloric acid upon the precipitate in the filter. The resulting red-violet solution gives the two bands of acid hematoporphyrin. (Compare Fig. 233, No. 6, p. 545.) Supersaturation with ammonia turns the solution yellowish, and the four bands belonging to hematoporphyrin in alkaline solution appear in the spectroscope.

DETECTION OF BILIARY PIGMENTS

The most important biliary pigments are bilirubin and biliverdin. The latter is derived from the former by oxidation in the spontaneous decomposition of bile by putrefaction, and perhaps also by ferments (oxydases). These two pigments, and more especially bilirubin, always appear in the urine whenever biliary pigment gets into the blood, *e. g.*, in jaundice (p. 42 et seq.). The oxidation products of bilirubin and biliverdin which may also appear in the urine are bilifuscin and biliprosin. These substances are not well characterized.

Icteric urine can usually be recognized by its color, which varies from a dark yellowish red or brown to a greenish black. A yellowish foam and yellowish stains of the urine upon clothes are particularly characteristic. The sediment also is usually stained yellow.

The following methods are employed chemically to demonstrate the presence of biliary pigments:

Gmelin's Test.—Filtered urine is allowed slowly to trickle down the side of a test-tube and stratify itself upon a layer of nitric acid. If biliary pigments be present, color changes occur at the line of junction of the two fluids—from greenish blue through violet red to yellow. The individual layers of urine pass through this play of colors with varying rapidity, according to their distance from the nitric acid, so that we usually see several of the colors superimposed. Sometimes the green ring is the only one we can see plainly, but this is usually enough. A red-violet[4] alone, however, may be produced by skatol or indol coloring-matters (p. 582). Gmelin's reaction depends upon the various steps in the oxidation of bilirubin; hence, the nitric acid should contain some nitrous acid. Crude yellow nitric acid fulfils this qualification, or the

[1] Cf. Schulte (Quincke's clinic), Deut. Arch. f. klin. Med., 1897, vol. lviii, parts 4 and 5.

[2] Centralbl. f. inn. Med., 1903.

[3] Zeit. f. physiol. Chemie, 1891, vol. xv. Cf. also Hammarsten, Skand. Arch. f. Physiol., 1891, vol. iii.

[4] Compare below with regard to the possibility of confusion with indican.

pure nitric acid may be employed if it be first heated with some organic substance, *e. g.*, some bits of wood. Both bilirubin and biliverdin react to Gmelin's test; only with biliverdin the reaction is abbreviated, as it were, because the biliverdin is already the partially oxidized green product, to which bilirubin must be changed as the first step in the process of oxidation.

Rosenbach's Modification of Gmelin's Test.—Icteric urine is filtered after having been acidulated with hydrochloric acid, and nitric acid is then dropped upon the paper. The play of colors which surrounds the drops of nitric acid will demonstrate even very slight traces of bile-pigment.

If this modified test be doubtful, the bile-pigment may be first extracted with chloroform. About 2 cc. of the latter and 3 drops of hydrochloric acid[1] are added to a test-tube almost filled with urine. The two liquids are then intimately mixed, but without violent shaking. The chloroform takes up the bile-pigment and becomes yellow; but the solvent will not settle readily if the mixture be shaken vigorously. The chloroform is now separated from the supernatant urine and an equal volume of water and a few drops of sodium hydroxid are added, and then mixed by repeatedly inverting the tube. The pigment will then be dissolved by the water, because the salt combination of the pigment is insoluble in chloroform. Gmelin's test can now be employed with this concentrated solution of bile-pigment. It will also succeed, though not so well, if tried on the chloroform extract. The least trace of an aqueous solution of iodin in potassium iodid or a drop of diluted ferric chlorid solution will gradually turn the chloroform extract green. The bile-pigment may also be demonstrated as microscopic crystals by evaporating the chloroform extract in a watch-glass. (Compare Fig. 278, *d.*)

Recently, Jolles has described a procedure which he claims increases the delicacy of Gmelin's reaction. It is as follows: 50 cc. of urine are shaken in a separatory funnel with 5 cc. each of a 10 per cent. barium chlorid solution and chloroform. Part of the bile-pigment will be extracted by the chloroform and part precipitated by the barium chlorid. The precipitate and the chloroform are separated from the urine and the chloroform evaporated upon a water-bath. A little yellow nitric acid is now added to the residue, and Gmelin's characteristic play of colors appears immediately.

In Gmelin's test nitric acid may, of course, bring out an indican reaction (p. 580). The blue of the indigo mixed with the yellow of the urine pigment will produce a green tint, and so may simulate Gmelin's reaction. But the indigo ring always has a blackish shade and consists of a fine precipitate. In a doubtful case the question may be settled by first isolating the bile-pigment by chloroform extraction (see above) and then performing Gmelin's test. This method is also necessary before we can be sure that both indican and bile-pigment are present. (See also the following test of Huppert-Salkowski.)

The presence of protein in the urine, as a rule, does not interfere with Gmelin's test unless the amount of bile-pigment is very small. In such an event it is better to first extract the bile-pigment with chloroform. The test cannot be well performed with urine from which the protein has been removed, because the precipitated albumin will carry a small amount of bile-pigment with it.

In some cases the test for bile is more delicate in urine containing albumin, for the coagulated protein becomes greenish in color. The ease with which biliary pigments are detected in blood-serum has led the author to add egg-albumen to urine suspected of containing bile. The compact coagulum shows a distinct green color.

Instead of underlaying the urine with nitric acid, the reagent, pure or diluted with water, drop by drop, may be added to the urine. When bile-pigment is present, one often obtains a characteristic coloration similar to that obtained in Trousseau's iodin test. The dilution diminishes the oxidative action of the acid.

Test with dilute acetic acid. With urine containing small amounts of biliary pigment one sometimes obtains a distinct reaction when acetic acid is added to the urine. The test is often positive with urine which does not yield a test with other

[1] The object of acidity is to free the bile-pigment (the latter reacts chemically as an acid) from the alkaline combination in which it occurs in the urine. In this way the extraction is rendered more complete, because free bile-pigment is insoluble in water, but readily soluble in chloroform, while the reverse is true of the salt of the bile-pigment.

reagents. On the other hand, the test may fail when bile-pigments are undoubtedly present. As icteric urine often becomes colored on standing in the air, one must assume that the action of the acetic acid is in the nature of a katalysis.

Huppert-Salkowski Test.—The urine is rendered alkaline by the addition of a few drops of a sodium carbonate solution; a solution of calcium chlorid (1: 10) is then added drop by drop, until the solution above the precipitate shows, after thorough mixing, the normal color of the urine. The precipitate is then filtered, well washed, placed in a test-tube with alcohol, and then dissolved by adding hydrochloric acid and shaking. If the clear solution contains bile-pigment, boiling will turn it green; if not, the fluid will not change color. The green solution will change to blue, violet, and red. This test is often successful when Gmelin's test gives no reaction, and Salkowski recommends it particularly in those cases where the indican in the urine interferes with Gmelin's test.

Trousseau's Test.—A few drops of tincture of iodin are added to the urine. If bile-pigment is present, the specimen will turn a beautiful emerald green. If the tincture of iodin is diluted ten times with alcohol, and the dilution is then stratified upon the urine, a green ring will appear at the line of junction of the two fluids.

Hammarsten's Test.[1]—A mixture of 19 parts of 25 per cent. HCl and 1 part of 25 per cent. HNO_3 is allowed to stand at room temperature for from several hours to a day, until it has turned slightly yellowish. One part of this acid mixture is added to 5 parts of 95 per cent. alcohol. A few drops of urine are added to a few cubic centimeters of this acidulated alcohol. If the urine contains bile-pigment, a characteristic green color appears almost immediately, even at room temperature. The author considers the test sensitive, but not more delicate than Salkowski's.

Stockvis' Test for Cholecyanin (*Bilicyanin*).—Five to 10 cc. of a 20 per cent. solution of zinc acetate are added to 20 or 30 cc. urine. Sodium carbonate solution is added slightly to diminish the marked acidity. The abundant precipitate will contain all the bile-pigments; it is washed on a filter and then dissolved in a little ammonia. This transforms the bile-pigment into cholecyanin. A neutral solution of the latter is blue green, and exhibits red fluorescence and a characteristic spectrum with three absorption-bands. One of these bands is in red, sharply outlined and dark, between C and D, nearer to C; a second, less sharp, in yellow, covering D; and the third, a very faint one, in green, between D and E.

Haycraft claims that in urine which contains bile-pigment powdered sulphur will immediately, or almost immediately, sink to the bottom. This peculiarity is even more characteristic of urine which contains biliary acids. The test is not very accurate, since after a certain time some of the powdered sulphur will sink in normal urine. It is probable that the temperature of the urine has something to do with the result of the experiment, but it has not been determined to what extent.

Krokiewicz' Reaction.[2]—One cc. of a 1 per cent. solution of sodium nitrite and 1 cc. of a 1 per cent. solution of sulphanilic acid are mixed, and added drop by drop to 0.5 cc. of urine. The amount added must not exceed 10 drops. The mixture becomes bright red, changing to amethyst on the addition of 1 or 2 drops of concentrated hydrochloric acid and a large amount of water. If the urine contains much bile-pigment, it should be diluted.

Microscopic Detection of Bile-pigments.—The urine must contain a sufficient amount of bile-pigment. It is acidified with hydrochloric acid and allowed to stand for some time in the cold, after which bilirubin will be precipitated as bundles of microscopic needles colored intensely brown (Fig. 278, *d*). These little bunches of needles are often observed when icteric urine is evaporated to test for the presence of leucin or tyrosin (p. 605). The bilirubin needles are, however, much browner than tyrosin needles.

Method for Removing Bile-pigment from the Urine in Order to Perform Other Tests.—The color of bile-pigment may be removed very easily either by extracting the acidified urine with chloroform or boiling the specimen with some animal charcoal. This is necessary before testing for salicyluric acid with ferric chlorid, because this reagent, like the tincture of iodin, is apt to produce a green discoloration in icteric urine, which hides the violet color of the iron salicylurate. The urine must not be boiled too long with the charcoal, as the latter is apt to combine with the salicyluric acid. It is always advisable to make a control test, in order to be sure that the process of decolorizing has not destroyed the substance we are trying to detect.

[1] Skand. Arch. f. Physiol., vol. ix, p. 313; ref. in Centralbl. f. Physiol., vol. xiii, p. 644.

[2] Münch. med. Woch., 1906, No. 11.

DETECTION OF BILE ACIDS

The bile acids occur in the urine chiefly in cases of obstructive (retention) jaundice. These acids should be isolated before we attempt to test for them.

Hoppe-Seyler[1] gives the following directions: Lead acetate and a little ammonia are added to the urine. The resulting precipitate is washed with water, then boiled with alcohol, and filtered while hot. The lead salts of the bile acids dissolve in hot alcohol. A few drops of soda solution are added to this solution, which is then evaporated over a water-bath until dry, and the residue boiled out with absolute alcohol, when the sodium salts of the bile acids dissolve. The filtered alcoholic extract is evaporated to a small volume, then precipitated, and allowed to stand with excess of ether in a closed bottle. In this way the sodium salts of the bile acids can often be obtained as crystals. But it is not necessary to wait for them, as the resinous precipitate may be dissolved immediately in a little water, and Pettenkofer's test applied. Thierfelder suggests that the urine be evaporated to a small volume, and the residue extracted with alcohol. The filtrate is evaporated, and the lead precipitate produced in the residue.

Tyson's process is simpler (Emerson, Clinical Diagnosis, 1906). One hundred and eighty to 240 cc. of urine are evaporated to dryness on the water-bath. The residue is extracted with absolute alcohol, and to the extract 12 to 14 volumes of ether are added. The biliary acids are precipitated, then are filtered off, dissolved in water, and the aqueous solution decolorized with animal charcoal.

Pettenkofer's Test.—To the solution of the bile salts we add two-thirds of its volume of concentrated sulphuric acid very slowly, so that the mixture does not become heated above 60° C. Then we add 3 to 5 drops of a solution of 1 part of cane-sugar in 4 or 5 parts of water, and shake, whereupon the liquid turns a beautiful violet color.

Strassburg[2] has at times succeeded in demonstrating the presence of bile acids in the urine directly by adding a small amount of cane-sugar and then filtering. To the dried filtrate is added a drop of pure concentrated sulphuric acid. If bile acids are contained in the urine, a beautiful violet spot appears within a quarter of a minute in the particular place at which the drop was added. This spot soon turns to a dark purplish red, which is particularly plain by transmitted light.

Von Udránsky considers a direct detection sometimes possible. He dilutes 1 drop of urine with 1 cc. of water and 1 drop of furfurol water (obtained by shaking 1 drop of furfurol thoroughly in one-half test-tube of water), and then adds 1 cc. of concentrated sulphuric acid. A violet color is formed. The author believes that it is unsafe to trust to the color reaction without previously isolating the acids, as the shades of color which are given by normal urines and those containing biliary acids are difficult to differentiate.

Haycraft claims that his method for determining the presence of biliary acids is perfectly trustworthy. This consists in shaking flowers of sulphur on the surface of the urine. In the presence of biliary acids the powder sinks to the bottom inside of five minutes. This phenomenon is probably due to the influence of the bile salts on the surface tension of the urine. This has possibly a connection with the emulsifying action of the bile. The test is of limited value, for urines containing bile-pigments possess the same property to a lesser degree (see p. 577), and urines examined for biliary acids usually contain bile-pigments. Moreover, the test does not react sharply in distinguishing normal urines. (See p. 577, Detection of Biliary Pigments.)

[1] Handbuch der physiol. u. path.-chem. Analyse, 1893, p. 378.
[2] Arch. f. d. ges. Physiol., vol. iv, p. 461.

DETECTION OF INDICAN AND INDIGO

Indican, or indoxyl-sulphuric acid, in the urine is the product of the putrefaction of proteins, and is a derivative of indoxyl, which in turn is an oxidation product of indol. This decomposition occurs in the intestine normally, but is more pronounced in digestive disturbances with diminished peristalsis (intestinal obstruction). Indican may also be found under some circumstances in various other parts of the body from suppurative processes. The substances from which indol and indican are derived is probably tryptophane, which is formed in the digestion of proteins. Indican is always present in the urine in small amounts.

An increased amount of indican in the urine is of some diagnostic importance in helping to locate the seat of an intestinal obstruction. Experience has shown that an *obstruction in the small intestine* is quickly followed by a marked increase in the amount of indican in the urine, as contrasted with an *obstruction in the large bowel,* where there is very rarely any such increase, unless perhaps in the later stages. This is probably because the trypsin of the pancreatic juice favors decomposition and the formation of indican. Both factors aid each other in the decomposition of the proteins. In deep-seated obstruction in the large intestine the stagnation of the contents, which favors decomposition, occurs primarily where trypsin is no longer active. (The latter, as is well known, is destroyed or reabsorbed in the course of the intestine.) In obstruction in the small intestine the stagnation takes place where the trypsin favors the decomposition. A further explanation is that the greater portion of the proteins which furnish the indican have been already absorbed in the large intestine.

Besides interference with the permeability of the intestine, one finds increased indican excretion in enteritis, typhoid, and especially in peritonitis (perityphlitis). The condition of the patient is in inverse ratio to the amount of indican in the urine.

Increased indican is also found in tuberculous conditions, not only those associated with the breaking down of tissue, but in tuberculous pleurisy and adenitis. Whether this is directly connected with the tuberculous condition or is due to an associated disturbance of digestion cannot be said. The former seems to the author to be possible, for indicanuria has been found in patients in whom the digestion was apparently normal. This observation seems to have a certain amount of diagnostic value.

Constipation only causes indicanuria when putrefactive processes take place. Indicanuria is not found in simple chronic constipation. In this condition resorption is usually above normal.

A certain amount of diagnostic significance is attached to the appearance of indicanuria in conditions in which protein is being broken down in other parts of the body than the intestinal tract. To this class belong the tuberculous conditions mentioned above. Increased indican is also seen in gangrene of the lungs, putrid bronchitis, and empyema. It is, however, not safe to assume the formation of pus from this sign, for the author has observed a pronounced indicanuria in tuberculosis with a serous exudate, associated with hyperpyrexia.

If the duct of the pancreas be occluded, the amount of indican in the urine will be diminished. However, as the indican in the urine is normally quite small in amount, or even absent altogether, a dimi-

nution can be clinically significant of an occlusion of the pancreatic duct only under conditions which would ordinarily favor the production of a large amount of indican, *e. g.*, jaundice and a meat diet.[1]

We can frequently demonstrate indican in normal urine by one of the following methods. They depend upon the fact that oxidizing agents transform indican into indigo. The reaction must be very striking to enable any safe diagnostic conclusions (as to increased intestinal decomposition or any other process or decomposition in the interior of the body, or as to the location of an obstruction).

Jaffe's Indican Test.—One-quarter of a test-tube of urine is mixed with an equal volume of concentrated hydrochloric acid, and a drop of a half-saturated solution of commercial chlorid of lime (chlorinated lime) is added. If no reaction takes place immediately, more of the chlorid of lime solution is added, drop by drop, without shaking. If the urine contains considerable quantities of indican, a blue-black ring of precipitated indigo will appear in the upper part of the tube, at the lower zone of action of the chlorid of lime solution. This ring will become more intensely colored upon standing. If a very large amount of indican be present, the entire fluid will turn black. We must be very careful not to add too much of the chlorid of lime solution, since in that case the *indigo* formed by the oxidation of the *indican* will become further oxidized to yellow *isatin*. Protein, if present, should be first removed by boiling and filtration. The indigo formed in this way will dissolve in a few cubic centimeters of chloroform by gentle agitation, coloring the latter blue. If only a small amount of indican be present, there is considerable danger of adding too much chlorid of lime. Hence the test has been modified at the Bern Clinic in the following way: First, a few cubic centimeters of hydrochloric acid are poured into a test-tube and a drop of the chlorid of lime solution is added. The mixture is well shaken, and then the urine is carefully stratified upon it, either by letting the urine flow down the side of the tube or, better still, by letting it fall upon the surface of the hydrochloric acid, drop by drop, through a filter. The indican reaction will then be shown very beautifully at the line of junction of the two fluids.

Obermayer's Test.—Obermayer[2] claims that he can avoid the danger of excessive oxidation, which is a defect in Jaffé's test, by the use of ferric chlorid as an oxidizing agent instead of chlorid of lime. He adds to the urine a small amount of a

[1] [The qualitative tests for indican seem to be among the most significant employed in urinary analysis. The amount of indican found in the urine in normal individuals is either not detectable by the ordinary tests or is, at the most, a mere trace.

On the other hand, when excessive putrefaction takes place in the intestine, or when suppurative processes are occurring, the urine may contain so much indican that the chloroform extract will be almost black in color. This condition calls for immediate attention on the part of the clinician, and it will be found, when steps are taken to unload the bowel, that the indican will decrease in amount or disappear. It is often found that symptoms of autointoxication are present coincident with the appearance of increased indican in the urine. These disappear when the cause leading to indicanuria is removed. It would also appear that in certain disturbed states of metabolism the production of indican in the organism leads to symptoms of intoxication which are not produced when the individual is otherwise normal. It is for this reason that one sometimes finds a large amount of indican in the urine with no positive subjective symptoms, and, on the other hand, the appearance of indican in other patients will be accompanied by acute exacerbations of a condition. This is sometimes seen in certain affections of the skin.—C. G. L. W.]

[2] Wien. klin. Woch., 1890, No. 9.

20 per cent. solution of basic lead acetate, in order to precipitate those substances which prevent the shaking out of the indigo by the chloroform. After removing the precipitate by filtration, he adds an equal volume of fuming concentrated hydrochloric acid, which contains 4 gm. of ferric chlorid to the liter. The mixture is then shaken. The reaction will take place, he claims, within a few moments, and the indigo may then be extracted with chloroform. Obermayer believes that this process is adapted for an accurate colorimetric determination of the amount of indican present.

Amann's Test.—J. Amann[1] recommends sodium pyrosulphate ($Na_2S_2O_7$) as an oxidizing reagent. He claims that this reagent also will not cause any loss of indigo by excessive oxidation. The test is performed as follows: To 20 cc. of urine are added a few drops of pure sulphuric acid, 5 cc. of chloroform, and then 5 cc. of a 10 per cent. solution of sodium pyrosulphate. They are mixed gently for several minutes (too much shaking may produce an emulsion). The chloroform is then allowed to settle and will be colored blue by the indigo. The method can be utilized for an exact colorimetric determination.

Gruber's Test.[2]—A test-tube is filled with 1 volume of the urine and 2 volumes of hydrochloric acid. Two or 3 drops of 1 per cent. osmic acid solution are added, and the mixture shaken. The urine is colored in a few minutes violet to blue. The indigo may be shaken out with chloroform. Osmic acid may further change the indigo to a colorless substance. Highly colored urines may be clarified with basic lead acetate.

Other oxidizing reagents often produce a more or less distinct indican reaction, *e. g.*, nitric acid in the test for bile-pigments. (See p. 575.) In the employment of nitric acid for the detection of indican there is great danger of decolorizing the indigo. It will be recalled that the decolorization of indigo is one of the reactions of nitric acid, which is therefore not a reliable agent for the detection of indican.

As already mentioned, *indican* is sometimes oxidized spontaneously to indigo in the urine before or after being voided. Urine which contains indigo presents a black, green, or bluish tint. All that is necessary to prove that the color is due to indican is to shake the urine with chloroform and then allow the latter to settle, when it will be seen to have turned blue. The needle-shaped or thin, plate-like crystals of indigo may sometimes be detected microscopically in the urine sediment, or even in the residue of the dried chloroform extract.

PRESENCE AND DETECTION OF PHENOL

Traces of phenol in the form of phenyl sulphuric and phenol glycuronic acids are normally present in the urine. After the administration of phenol, the amount is largely increased, and this is more pronounced when resorption through exposed surfaces has occurred from the use of carbolic dressings. Pathologically, phenol is increased in the urine on increased intestinal putrefaction and in pus-formation. Brieger found it in empyema. Blumenthal believes that fever itself causes increased phenol formation. This observer claims that the amount of phenol in the urine of patients suffering from typhoid allows one to judge the amount of decomposition occurring in the intestine, and that in tuberculosis an increased amount of phenol points to an intestinal tuberculosis. The detection of phenol in the urine and the approximate estimation of the amount is given on p. 611. The blackish green color of urine containing phenol is described on p. 555.

Concerning the quantitative estimation of indican see p. 643.

[1] Revue med. de la Suisse Rom., 1897, No. 6, p. 499.
[2] Münch. med. Woch., 1905, vol. xxxiii.

ROSENBACH'S REACTION (RED INDOL AND SKATOL PIGMENTS)

Rosenbach[1] has described the following reaction. Concentrated nitric acid is added drop by drop to a test-tube of urine while it is being continually boiled. The urine gradually assumes a Burgundy-red color, while the foam produced by shaking turns a bluish red. A reddish or brownish-red color without the foam becoming violet red is not distinctive, as it may be due to the urobilin in the urine. Continued addition of nitric acid will turn the red color rather rapidly to a yellowish red or yellow with a yellow foam. The addition of a solution of soda or ammonia drop by drop will cause a bluish-red precipitate, which dissolves in an excess with the formation of a reddish-brown color. In these cases the urine is sometimes already of a reddish shade, or sometimes a slight reddish tinge occurs upon the addition of nitric acid while the specimen is still cold. The reaction seems to depend principally—although perhaps not exclusively—upon the formation of indigo-red (indirubin, indigo-purpurin), an oxidation product of indoxyl or indican. (See p. 579.) It may too, perhaps, depend upon the formation of skatol pigments by means of the oxidizing influence of nitric acid. Indigo is often produced in this way—hence the violet shades of the reaction. The test has a diagnostic importance similar to that of the indican reaction.

DETECTION OF MELANIN (PHYMATORRHUSIN) AND MELANOGEN

A peculiar brownish-black coloring-matter, the so-called melanin (phymatorrhusin), sometimes appears, partly as such, partly as a colorless chromogen, in the urine of patients suffering with melanotic neoplasms. Urine which contains melanin is blackish. Exposure to the air and oxidizing agents, such as nitric acid or ferric chlorid, will turn it still darker. Urine which contains colorless melanogen exhibits a dark color only after the melanogen has been changed by these agents into melanin. The addition of bromin water and sulphuric acid or chlorin water also produces a dark color. An excess of bromin or chlorin water will cause a decolorization and throw down a dense dirty-yellow precipitate. Boiling with fuming nitric acid will, under certain circumstances, decolorize melanotic urine. Melanin may be confounded with indigo, and melanogen with indican. (See p. 579 et seq.) The solubility of indigo in chloroform, and the resulting blue color, will serve to differentiate them.

UROROSEIN (URRHODIN)

A red color is not infrequently noticed in the urine, appearing soon after the addition of mineral acids, especially hydrochloric acid. It occurs both in health and in many conditions of disease. Nencki and Sieber recognized it as due to a pigment which they called *urorosein*, the chromogen of which is contained in the urine. It is probably identical with the pigment described by Heller as *urrhodin*, evidently differs from indigo-red, and may possibly be a derivative of skatol. In contrast to Rosenbach's reaction (indigo-red, above), the red color disappears upon the addition of alkaline carbonates to the urine. This pigment, unlike indigo-red, is insoluble in chloroform and ether.

UROERYTHRIN

This pigment occurs in normal urine, particularly after the ingestion of large quantities of food and alcohol, and after profuse perspiration; it is also found in pathologic urines in digestive disturbances, in gout, and in febrile conditions. This is the pigment which is responsible for the beautiful rose tint in many of the uratic sediments. It was formerly regarded as identical with urorosein, but is now known to be a different substance. Urines containing large quantities of this pigment are of a decided orange color. When concentrated sulphuric acid is added to the pigment, a carmin-red color is produced; alkalis (not ammonia) change the color

[1] Berlin. klin. Woch., 1889 and 1890.

of the pigment first to a purplish blue and then to a green. These reactions obtain only with pure solutions of the pigment, however, and such solutions are difficult to obtain. The coloring-matter is soluble in amyl alcohol and bleached on exposure to light.

DETECTION AND OCCURRENCE OF UROBILIN AND UROBILINOGEN

Urobilin is in all probability a derivative of bilirubin. Modern investigations have, however, cast doubt upon the old assumption that it was identical with hydrobilirubin. Urobilin ocurs in small amounts even in normal urine, but, according to Saillet, not until the urobilinogen has been acted upon by light. The normal yellow color of the urine is not due to urobilin, but to urochrome.

Clinically, the detection of urobilinogen has the same significance as that of urobilin. According to the investigations of F. Müller, urobilin is formed from biliary coloring-matters in the intestine. Whether it can be formed directly from the coloring-matter of the blood is not known. Hildebrandt describes a case in which there was total occlusion of the ductus communis choledochus and a severe jaundice. There was the resorption of an enormous hematoma. During this time there was no urobilin in the urine or other fluids of the body. He concludes that neither the liver nor the other processes of metabolism were able to transform the coloring-matter of the blood directly into urobilin. It is, however, questionable if this is so in all cases.

Pathologically, urobilin is found in increased amount in many cases of jaundice (urobilin jaundice). The conditions for this are that some bile reaches the intestine (F. Müller). One also finds a large amount of urobilin in all affections associated with the breaking down of red cells, as in fever,[1] scurvy, internal hemorrhage, and pernicious anemia. It was at one time assumed that the urobilin was a direct transformation product of the breaking down of blood coloring-matter. It is now believed that the urobilin is formed from the biliary coloring-matters, as is normally the case, and is only excreted in the urine because in these cases the liver is incapable of transforming it to biliary pigment. (Disturbance of the intermediary circulation of urobilin between the liver and the intestine.) This is in accord with the modern view that in these cases the jaundice, which was previously assumed to be hematogenous, is also a sequel of insufficiency of the liver.

This view makes doubtful the diagnostic significance of the presence of urobilin in the urine as showing an internal hemorrhage. It was formerly thought that the blood coloring-matters were transformed into bilirubin and hematoidin, and were excreted as urobilin. Hence the detection of this substance was thought to indicate cerebral hemorrhage, hemorrhagic infarcts, retro-uterine hematocele, and extra-uterine pregnancy with internal hemorrhage. It must be noted that in all these cases a disturbance of the liver is not excluded, especially when the condition is associated with fever. For the recognition of cerebral hemorrhage the detection of urobilin in the urine loses much of its significance, as differentiating that condition from softening. Most of the hemorrhages of the brain are too small to cause a distinct increase of urobilin in the urine. The larger hemorrhages are too rapidly fatal to

[1] Hildebrandt, Zeit. f. klin. Med., 1906, vol. lix, has shown that the excretion of urobilin is not directly associated with fever, but is a result of conditions associated with hyperpyrexia, such as a severe infection or a toxemia.

show urobilin in the urine. The excretion of the substance would be expected at a time when the differential diagnosis between softening and hemorrhage has more theoretic than practical interest. In lesions of the brain, the fever which accompanies them may give rise to a urobilinuria.

Urine which contains a very large amount of urobilin is often very dark. This is not invariably the case, because urobilin does not possess very intense coloring properties. Usually, other pigments which may be increased in quantity along with it are principally responsible for the dark color. In fact, a very dark urine may contain very little, and a light urine a large amount of, urobilin.

DETECTION OF UROBILIN

The most accurate method for the demonstration of the presence of urobilin is by means of the spectroscope, after first acidifying the urine with a little hydrochloric acid to make the spectrum more distinct. Acid urobilin solutions, when very concentrated or in thick layers, absorb the entire blue end of the spectrum as far as the middle of green. On the other hand, a thin layer or a less concentrated solution shows an absorption-band between green and blue (Fig. 233). In contrast to urobilin, the biliary pigments proper absorb the spectrum diffusely. A simple chemical method for demonstrating the presence of urobilin is as follows: The urine is rendered strongly alkaline with ammonia, filtered, and a few drops of a 10 per cent. alcoholic or aqueous solution of zinc chlorid are added. A beautiful green fluorescence occurs if urobilin be present.

To demonstrate chemically a very small quantity of urobilin in the urine it must be first extracted by gently shaking a specimen of urine, acidulated with a few drops of hydrochloric acid, with one-third its volume of amyl alcohol. When the alcohol has extracted the urobilin, it will be colored brown. If the layers be not distinct and the amyl alcohol portion remain cloudy, like an emulsion, the separation and the clarifying may be aided by the addition of a few drops of ethyl alcohol. Several drops of an alcoholic ammonium chlorid solution (spiritus Dzondii) and some 1 per cent. alcoholic solution of zinc chlorid are then added to the amyl alcohol layer, and the resulting fluorescence shows the presence of urobilin.

Hildebrandt recommends as being more delicate the modified test with zinc acetate. The reagent is an unfiltered solution of 10 parts of zinc acetate and 90 parts of absolute alcohol. The reagent is shaken before using. Equal parts of the reagent and the urine are mixed, and the precipitate which is formed filtered off. With an increased amount of urobilin the filtrate shows a distinct green fluorescence, either directly or after the addition of ammonia. The spectrum shows the characteristic absorption-bands. The advantage of the method is that the large amount of zinc salt added precipitates albumin and other urinary substances which interfere with the reaction. The bilirubin in the urine does not interfere with the reaction. With a large amount of bilirubin in the urine, Schlessinger recommends its removal by adding to the urine one-quarter of its volume of 10 per cent. calcium chlorid solution, neutralizing carefully with ammonia, and filtering off the precipitate containing the biliary coloring-matter.

Whether the urobilin, as characterized by the above-mentioned tests, is a specific substance, or whether there exist several urobilins, has been recently much discussed.[1] A final verdict is not yet possible. In any case a differentiation (suggested by Jolles) of physiologic and pathologic urobilins has not been sufficiently worked out to be of any clinical value. Hildebrandt has recently returned to the view that urobilin is a definite chemic substance.

Tests for Urobilinogen

Hildebrandt uses the Schlessinger test described above, by allowing the urine and the reagent to stand for twenty-four hours in order to effect the conversion of urobilinogen into urobilin. If the fluorescence is only to be observed after the urine has stood, urobilinogen is alone present. If a fluorescence is obtained at once, which increases after twenty-four hours, both substances are present in the original urine.

The Paradimethylamidobenzaldehyd Reaction.—O. Neubauer[2] showed that the reaction which was first described by Ehrlich was due to the presence of urobilinogen, after Pappenheim had demonstrated that the substance was constantly present with urobilin. Clemens, Thomas, and Hildebrandt are those who have done the most work with this reaction.

According to Hildebrandt,[3] the reaction is carried out as follows: 20 gm. of paradimethylamidobenzaldehyd are rubbed up in a mortar with 100 cc. of concentrated hydrochloric acid, more acid added, until the volume is 500 cc., and then the whole made up with water to 1000 cc. Two drops of the reagent are added to the urine. If the urine contain urobilinogen, it becomes dark red in color, and shows a band in the orange-yellow between D and E. Occasionally the red color only appears after some minutes or after the urine has been heated. The spectroscopic examination is absolutely necessary for the test.

K. Thomas has shown that the "bright yellow" reaction which occurs with the diazo test described on p. 607 is due to urobilinogen. The reaction is less delicate than the paradimethylamidobenzaldehyd reaction.

QUALITATIVE DEMONSTRATION OF GRAPE-SUGAR (GLUCOSE; DEXTROSE)

Preparation of the Urine for the Qualitative Test for Sugar

Very small amounts of glucose probably occur in every normal urine. We have no simple reaction to prove this absolutely, but we do know that normal urine reduces less after than before fermentation by yeast. Pathologic amounts of sugar can, on the contrary, be demonstrated by very simple methods. We must, in the first place, discriminate between a permanent or persistent glucose excretion (*diabetes mellitus*) and one of the transient type (*glycosuria*). No sharply defined distinction can as yet be drawn between these two. *Glycosuria* accompanies various disorders, particularly cerebral and digestive affections, certain forms of poisoning (morphin, carbon monoxid, chloral hydrate, oil of turpentine (in the two latter cases the presence of glycuronic acid is responsible for the condition), corrosive sublimate, amyl nitrite, nitrobenzol, curare, phloridzin, etc.), and prolonged hunger. It sometimes happens that otherwise perfectly healthy people temporarily excrete glucose in the urine after too abundant ingestion of sugar or of other carbohydrates (*alimentary* or *physiologic glycosuria*).

It is, however, quite essential to distinguish cases of *alimentary glycosuria* due merely to excessive ingestion of sugar from those attributable to undue consumption of starches. The latter presumably indicate some grave disorder, because the tolerance for starches is much greater than for sugar, probably for the reason

[1] Cf. Jolles, Centralbl. f. inn. Med., 1895, and Pflüger's Arch., vol. lxi, pp. 623–637; and Archibald S. Garrod and F. Gowland Hopkins, Jour. Physiol., vol. xx, pp. 112–114.

[2] Sitzungsbericht d. Ges. f. Morphol. Physiol., München, 1903, H. 2.

[3] Zeit. f. klin. Med., 1906, vol. lix.

that the absorption of starch takes place much more slowly. Hence, when abundant starch ingestion gives rise to sugar excretion, we may best consider the case as related to diabetes mellitus, and reserve the term "*physiologic* or *alimentary glycosuria*" for cases where the starches can be freely ingested without exciting sugar excretion, but where excessive ingestion of sugar occasions a glycosuria. As a matter of fact, excessive ingestion of sugar may overstep the tolerance of perfectly healthy individuals.

Urine containing much glucose is peculiar in presenting a light or pale color combined with a high specific gravity. In *true diabetes* the amount of urine is usually, although not always, increased. Hence a pale urine, excreted in excess of the normal daily quantity, and with a specific gravity of 1030 or more, allows of the most decided suspicion of diabetes mellitus. Urine containing glucose ferments spontaneously after standing for some time. This characteristic alcoholic fermentation may be recognized either from the development of carbonic acid bubbles or from the microscopic demonstration of yeast in the sediment. Therefore sugar tests must always be performed with a fresh specimen.

To detect a small quantity of glucose in a doubtful case we naturally select for examination a specimen voided during the day and a short time after eating, because the quantity of sugar is apt to be then at a maximum. If the meal was rich in starch or sugar, we are still more liable to obtain a positive result. Of course, we must remember that apparently perfectly healthy people may excrete sugar after too abundant consumption of these two foods. If an excessive ingestion of starch alone produces glycosuria in such people, they may be considered as on the border-line between health and diabetes mellitus.

If the urine contain protein, this must be removed before proceeding with the tests for sugar. (See p. 566.) If it contain hydrogen sulphid (hydrothionuria, see p. 555), this compound may be removed by shaking the urine with lead carbonate and filtering.

Almost all the qualitative tests for sugar are most successful when the acid urine is precipitated with lead acetate. About 5 cc. of a solution of basic lead acetate are added to 50 cc. of urine; the mixture is filtered, and the excess of lead removed from the filtrate by the addition of several cubic centimeters of a saturated solution of sodium phosphate, this solution being added until precipitation no longer occurs. The decolorized filtrate is then employed for the tests, and is better adapted for this purpose than the original urine, since various substances which might have interfered with the reactions have been removed. The original urine must be distinctly acid, and also remain acid after the addition of the sodium phosphate, since sugar is precipitated from an alkaline urine by the addition of lead. The acid reaction should be finally insured by the addition of several drops of acetic acid. All concentrated urines should be diluted with 2 or 3 volumes of water, in order to minimize the effect of certain substances which interfere with the reactions.

An appropriate preparation of the urine for the qualitative sugar tests is also the treatment with mercuric nitrate, as recommended upon p. 625 for the polarimetric examination.

Glucose may be detected in the urine by the following chemical tests:

Moore-Heller's Test

A few cubic centimeters of potassium or sodium hydroxid are added to about three times this volume of urine in a test-tube and then boiled. If considerable sugar be present, the mixture will turn a dark brown as a result of the oxidation of the glucose. The chemical reaction upon which this test is based has not yet been definitely ascertained. The

reaction is absolutely characteristic of sugar only when the color becomes dark brown or, at least, yellowish brown, or, with a diluted urine, an intense clear yellow. The test is rather delicate, a characteristic reaction being obtained even with a considerably diluted diabetic urine. Unless the result is absolutely certain, it is a good plan to compare the reaction with that obtained from a normal urine, and in doubtful cases even with that from a diluted urine. If the mixture of diabetic urine and potassium hydroxid be allowed to cool, and is then cautiously acidulated with sulphuric acid, an odor of burnt sugar should be developed.

Reduction Tests

Trommer's, or the Copper Test.—One-third the volume of potassium or sodium hydroxid is added to the urine in a test-tube, and then drop by drop a solution of cupric sulphate (1 : 10), the mixture being shaken constantly until a slight excess of the precipitated cupric hydroxid remains undissolved. If sugar be present, we can add a good deal more of the cupric sulphate solution without producing a precipitate, and the mixture will turn a beautiful blue color. This depends upon the fact that in the presence of glucose the formation of an easily soluble double combination takes place, which holds much more cupric hydroxid in solution. The blue color does not, however, positively prove the presence of sugar, because it also occurs if the urine contain glycerin or tartrates, or if ammoniacal decomposition has set in. Urine which contains protein also holds some cupric hydroxid in solution, but here a violet color is produced. If we heat this dark-blue solution just to boiling in the presence of sugar, cuprous hydroxid ($Cu_2(OH)_2$) and cuprous oxid (Cu_2O) separate in greenish-yellow clouds, which gradually turn brick red and finally diffuse throughout the fluid. This is due to the fact that glucose has the power, in alkaline solution, to reduce cupric hydroxid to cuprous hydroxid and cuprous oxid. These separate out as a yellow to brick-red precipitate,[1] and the liquid becomes decolorized. If a large amount of sugar be present, metallic copper (Cu) may even separate out upon the side of the test-tube in the form of a brownish-red coating.

A *positive* and *typical* copper reaction certainly permits no doubt in regard to the presence of sugar in the urine, for no other substances occur in the urine which can furnish in every detail a corresponding reaction. At most, in some individual instances, it is only necessary to distinguish whether it is glucose or some other reducing carbohydrate that is present, and, from the much greater frequency of glucose, it is generally safe to attribute a positive copper test to it. To be perfectly certain that the reducing action is due to glucose, the test must always be controlled by other tests. In regard to the differentiation between the individual carbohydrates and the recognition of the copper-reducing combined glycuronates, which appear more or less abundantly after the ingestion of certain drugs (camphor, morphin, phenol derivatives, such as paracresol, also salicin, salol, thallin, chrysophanic acid, saccharin, santonin), and sometimes, under both physiologic and pathologic conditions, abundant skatol and indol formation, compare p. 611 et seq.

[1] Cuprous hydroxid is yellow; the oxid is brick red. The more alkaline the solution, the more pronounced the brick-red color, the oxid taking the place of the yellow cuprous hydroxid.

If the copper reduction be less typical, a reasonable doubt may arise as to whether the urine contains glucose or not, because normal urine, in virtue of the presence of uric acid, kreatin, kreatinin, and combined glycuronic acid, does reduce copper to a certain extent. In order to differentiate a reaction due to glucose from a similar one occasioned by one of the above constituents of the urine, the following distinction should be noted: If the reduction be due to glucose, the blue solution must not only be decidedly decolorized, but there must also be formed a distinct granular precipitate of cuprous oxid and cuprous hydroxid. On the contrary, the reduction by normal urine is never associated with the immediate formation of a yellow or brick-red precipitate, but there is produced merely a dirty yellowish fluid, because kreatinin, ammonium salts, and other substances keep in solution the small amount of cuprous oxid which is formed. It does often happen, however, that after allowing the test to stand for some time in the cold, normal urine will bring down a yellowish-red precipitate. Such a late separation is not suggestive of glucose. The above distinction in regard to the rapidity of reduction is in reality a quantitative test. Urine containing glucose keeps a much larger amount of cuprous hydroxid in solution, but is also able still further to reduce this soluble excess to the red suboxid, which cannot remain in solution. It is evident that the above is the real difference between urine containing sugar and one free from it, since, if the urine contain less than 0.2 per cent. of sugar, the reduction occurs just as in normal urine without precipitation, for the moderate amount of cuprous oxid will remain in solution. Heating urine which contains such slight amounts of sugar simply turns it yellow, but without any turbidity. Yet even in these cases we must acknowledge (and this is of some diagnostic importance) that the yellow color is very much more intense, clearer, and in a measure more translucent than with normal urine, very likely because the fluid contains a considerable amount of suboxid, despite the fact that it remains clear. In such instances, where Trommer's test produces a clear yellow color, a granular precipitate of the red suboxid usually appears a short time after cooling. By paying attention to these facts, an expert can frequently make use of such atypical reactions in recognizing a doubtful case of diabetes mellitus which has been influenced by the diet. Moreover, the reducing action of the normal urinary constituents may be prevented if we perform Trommer's test at a temperature of 60° to 70° C. This is a more certain method in doubtful cases, because at this temperature the normal constituents do not reduce to any noticeable degree. This temperature is easily obtained by first boiling the urine, then adding one-third its volume of cold potassium hydroxid, and then the cupric sulphate solution.

To make Trommer's test as delicate as possible, the first essential is to have as much cupric oxid as possible in solution, so that the abundantly reduced cuprous oxid may be precipitated. This end is accomplished, as already mentioned, by continuing to add cupric sulphate until a small amount remains undissolved. On the other hand, too much should not be added, because an excess of unreduced cupric hydroxid, when heated with potassium hydroxid, will become blackened from the formation of cupric oxid, and so very likely hide the reaction.

The delicacy of the test may sometimes be further increased by diluting the urine containing sugar two to five times. This dilution will diminish the power of the urine to dissolve the suboxid and will cause a granular precipitate to form where the undiluted urine gave no reaction. If the urine be free from glucose,

this dilution will not produce any change, because the slight trace of cuprous oxid which is formed will remain in solution in spite of the dilution.

Another method of improving the delicacy of Trommer's test is to shake the urine first with finely powdered animal charcoal, and finally filter. The animal charcoal evidently retains certain substances which dissolve the suboxid and prevent its precipitation.

Seegen's modification of Trommer's test can be recommended for the detection of very small quantities of sugar. It depends upon the fact that animal charcoal will absorb glucose while in solution, and that the latter can be washed out of the charcoal again. Seegen makes a thin paste with purified animal charcoal and the urine to be examined. A few minutes later this paste is poured upon a filter. After the urine has filtered through, he washes the charcoal remaining upon the filter-paper with as much water as he employed urine, and then repeats the process. The filtrate of each washing is kept separate, and Trommer's test is performed with each of these filtrates. The substances which cause the solution of the cuprous oxid will be retained in the carbon much longer than will the glucose. Frequently the test succeeds best with the second or third wash-water, as the first may contain too many of the substances which dissolve the suboxid. This method is very much more sensitive for urine which contains only a slight amount of sugar than Trommer's test upon the urine itself. Seegen claims that a positive reaction is absolute proof of the presence of sugar, because the second or third wash-water from a normal urine will no longer reduce.

The copper test may also be performed with *Fehling's solution*, such as is used for quantitative determinations. (See p. 619.) This should be freshly prepared each time before use; it consists of equal parts of solutions I and II. The test should be performed as follows: About 5 cc. of urine are first boiled in a test-tube, and allowed to cool for about twenty seconds; then about 1 cc. of Fehling's solution is added. If sugar be present, the reaction appears immediately. The reason we allow the specimen to cool off to about 60° or 70° C. is because at that temperature normal urine will no longer reduce. If an insufficient amount of copper be added, the cuprous hydroxid which is formed will not become precipitated, but will remain dissolved in a yellow solution. In such an event the test must be repeated with an increased quantity of Fehling's solution. Fehling's solution possesses no particular advantage for the qualitative test; on the contrary, the selection of exactly the amount of copper solution to procure a maximum precipitation of cuprous oxid is much more difficult with this than it is with Trommer's test, where the least excess of copper is easily recognized by the appearance of undissolved cupric hydroxid.

Protein in the urine does not interfere with the reduction of the copper, but it does hinder the precipitation of the red suboxid. For this reason the protein should be removed from the urine before performing the test. (See p. 566.) It is equally important to perform all copper tests with fresh urine, because the ammonium carbonate and the free ammonia formed in alkaline fermentation will also prevent the precipitation of red cuprous oxid.

Provided they are properly performed and the above precautions are observed, the copper tests are still the most practical and safest methods for the qualitative detection of sugar. Only a large amount of the other carbohydrates or of the salts of glycuronic acid can lead to confusion. (See p. 597 et seq. in regard to the appearance of the latter and its differentiation.) It should be remarked that after successful treatment of diabetes has caused the glucose to disappear from the urine, we often find large quantities of combined glycuronates present. The latter, however, can be easily distinguished from dextrose by the very tardy appearance of the copper reduction. In doubtful cases the tests yet to be described may serve as controls, particularly Almén-Nylander's, the fermentation test, and Rubner's test.

(*b*) **Almén-Nylander's Test (Modified Böttger's Test).**—The original Böttger test depended upon the reduction of bismuth subnitrate, $NO_3Bi(OH_2)$ by the glucose

in alkaline solution. But the test was not reliable until modified by Almén-Nylander. The reagent employed is prepared as follows: 4 gm. of Rochelle salt (potassium sodium tartrate (tartarus natronatus)) are dissolved in 100 cc. of 10 per cent. sodium hydroxid (specific gravity at 19° C. = 1.115) with gentle heat, and then as much bismuth subnitrate is added as will dissolve (about 2 gm.). After cooling we filter off with glass-wool any undissolved bismuth subnitrate which remains. If kept in a dark bottle, the reagent can be preserved for years. To the urine is added about $\frac{1}{10}$ its volume of the reagent, and the mixture boiled for a few minutes. In order to prevent the urine from boiling over and burning the fingers, a small coil of platinum wire may be dropped into the fluid, or the test-tube may be held to one side of the flame, so that violent ebullition shall not occur. If glucose be present, the fluid darkens and a black precipitate of suboxid of bismuth separates. If the solution turns dark only upon cooling, the test is not positive. A white precipitate of phosphate will be all that is formed upon boiling with urine free from sugar. If a very small trace of sugar be present, the precipitate of the phosphates may be seen to be grayish after it has settled. Nylander's test is delicate enough to indicate 0.025 per cent. of sugar. Uric acid and kreatinin, the reducing substances of normal urine, do not reduce the bismuth solution.

Before attempting Nylander's test we must first remove any protein from the urine, because an albuminous urine will produce a precipitate of sulphid of bismuth. With small quantities of protein the latter precipitate may be easily differentiated from the oxid of bismuth by its reddish-brown color. But if the protein contents of the urine are large, a brownish-black precipitate will appear, which can very readily be confounded with the glucose reaction. According to Zülzer, albumin, mercury, and chloroform tend to inhibit the reduction of the bismuth solution. If the urine be ammoniacal, the appearance of the reaction may be interfered with.

With the above-mentioned reservations, Nylander's is one of the most reliable of the sugar tests. It is always negative with normal urine, and so is particularly well adapted to decide a case where Trommer's test is doubtful. Considerable quantities of combined glycuronic acids or pentose will also plainly reduce Nylander's solution, and in doubtful cases these two substances must be excluded (according to p. 598) before we can assume that the urine contains sugar. The reduction of Nylander's reagent, which occurs after the ingestion of senna, of rhubarb, of eucalyptol, of kairin, of quinin, and of oil of turpentine, probably depends upon the presence of combined glycuronates. The senna and rhubarb urine turn red, due to the alkali contained in the solution.

Manifold Significance of the Reduction Tests

The following table, arranged by G. Brückner,[1] indicates the number of substances occurring in the urine, which may effect reduction in the tests of Nylander and Trommer, and the necessity of employing other methods of examination before concluding that such a reduction is positive evidence of the presence of glucose.

I. Normal urinary constituents which, according to their presence in larger or smaller amounts, may produce a varying degree of reduction or change of color of the earthy phosphates (in Nylander's test).

Trommer's Test.	*Almén-Nylander's Test.*
Traces of carbohydrates, as dextrose, isomaltose, pentoses, animal gum, glycuronic acid compounds.	
Pyrocatechin.	Uroerythrin.
Bile-pigment.	Urinary pigments (urobilin in particular) when present in greatly increased amounts cause a brownish discoloration of the phosphatic deposit.
Urinary pigment.	Indican.
Uric acid.	
Indican.	
Kreatinin.	
Urobilin.	
Urobilinogen.	

Concentrated urines are particularly apt to effect reduction, and the same is true of urines containing a moderate or large quantity of formed elements (leukocytes, erythrocytes, epithelial cells).

[1] Aerztliche Rundschau, 1899, No. 42–44.

II. Products of abnormal metabolism which effect reduction:

Trommer's Test.	*Almén-Nylander's Test.*
Hexoses (dextrose, levulose, isomaltose, lactose [in puerperal women.—Ed.]), pentoses, glycogen, increased quantities of glycuronic acid compounds.	
Homogentisic acid.	Blood-pigment. Increased quantities of hematoporphyrin. Homogentisic acid (weak).

III. Reducing substances added to the urine as preservatives, which consequently make the reduction tests for sugar impossible:

Trommer's Test.	*Almén-Nylander's Test.*
Formaldehyd. Chloroform.	

IV. Drugs or the derivatives obtained from them as the result of metabolic change:

Trommer's Test.	*Almén-Nylander's Test.*
Acetphenetidin.	Antipyrin.
Antifebrin.	Arbutin.
Arbutin.	Benzoic acid.
Benzoic acid.	Benzosol.
Benzosol.	Quinin (large doses).
Copaiba balsam.	Chloral.
Chloral.	Eucalyptol.
Glycuronic acid compounds of drugs. (See p. 597.)	Glycuronic acid compounds of drugs. (See p. 597.)
Morphin.	Indican.
Phenacetin.	Kairin.
Saccharin.	Rheum (also frangula and cascara sagrada).
Salicylic acid.	Salol.
Salol.	Senna.
Sulphonal.	Sulphonal.
Turpentine.	Turpentine.
Thallin.	Trional.
Urethan.	

Phenylhydrazin Test (Fischer-v. Jaksch)

Two drops of a concentrated solution of lead acetate are added to about 10 cc. of urine, and the precipitate filtered off; the filtrate is acidified with a drop of acetic acid; phenylhydrazin hydrochlorid, the size of a pea, and a piece of sodium acetate the size of a bean, are added. The mixture is heated for about a half-hour over a water-bath and then allowed to cool.

If glucose be present, a yellow precipitate separates out upon cooling. This consists of characteristic microscopic aggregates of needle-like crystals of phenylglucosazone (Fig. 236). If the precipitate be not crystalline or of a yellow color, or if the crystals are not of the form represented in the accompanying plate, we must not consider that the test is positive. The test is very delicate and even sufficient to indicate the presence of 0.01 per cent. of sugar in the urine. As a matter of fact, it is almost too delicate for clinical purposes, as under certain conditions the normal amount of sugar in a urine may give a positive reaction. Besides, there is a source of error in the test, since certain other substances that are normally found in urine may produce a similar reaction. By the determination of the melting-point of the osazone which is formed, a definite identification may be obtained, but this is too difficult for ordinary clinical methods. This is also the best method of distinguishing from the osazones of glucose the osazones of other carbohydrates which, though rarely, may be found in this test. Before performing the phenylhydrazin test, it is advisable to first remove the protein from the urine.

The phenylhydrazin test has been simplified by Cipollina[1] under Salkowski's

[1] Deut. med. Woch., 1901, No. 21, p. 334. The other modifications of the test (Neumann, Kowarski) are also mentioned and criticized here.

direction. Five drops of pure phenylhydrazin (the base), 0.5 cc. of glacial acetic acid, and 4 cc. of urine are mixed together in a test-tube. The mixture is heated over a small flame for about a minute, being carefully and constantly shaken so as to prevent bumping. Four or 5 drops of sodium hydroxid of a specific gravity of about 1160 are next added, but the fluid must still remain acid; this mixture is heated a moment more and then cooled. With this method of procedure, especially in the case of a urine of low specific gravity, the characteristic roset crys-

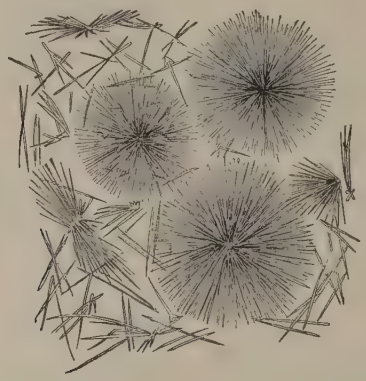


Fig. 236.—Crystals of phenylglucosazone (phenylhydrazin test for glucose) (after v. Jaksch).

tals appear immediately or, at least, within twenty minutes. In doubtful cases it is necessary to allow the test that amount of time. Thorn-apple crystals are not at all characteristic, but yellow balls which are gradually transformed into sheaths of needles are.

Rubner's Test[1]

Ten cc. of a concentrated solution of neutral lead acetate (1 part of lead acetate to 10 parts of distilled water) are added to 10 cc. of urine. The mixture is filtered, and ammonia carefully added to the filtrate drop by drop until a cheesy precipitate remains. The mixture is then heated over a water-bath to 80° C. During the heating, if glucose be present, the precipitate will become a beautiful rose or salmon red. The chemistry of this reaction is not positively known. The test is reliable, very delicate, and therefore particularly appropriate when Trommer's test seems doubtful. If the precipitate be heated too much, the color becomes brown, like café au lait, and is no longer characteristic. Milk-sugar gives a yellow-red to brown color. The author does not know how the pentoses and glycuronates react to this test.

Fermentation Test

Several of the above tests for glucose are sometimes uncertain unless the reaction is very characteristic, and often even when the result is positive.

Trommer's and Nylander's tests merely indicate the presence of a reducing substance, and do not prove that this substance is really glucose. If the reduction test result positively again and again with the same patient, and if, furthermore, the patient presents clinical appearances of diabetes mellitus (specific gravity, quantity of urine, and general appearance), the probability of glucose being present in the urine becomes, for all practical purposes, a certainty. But where the reducing substance appears temporarily, and when there are no further data for diagnosing diabetes mellitus, we need a more definite proof that the

[1] Zeit. f. Biol., vol. xx, p. 397.

reducing substance in question is some carbohydrate. Either Rubner's test, the phenylhydrazin test, or the fermentation test will answer this purpose. The last mentioned is one of the surest and most convincing of all sugar tests, and should be resorted to in all doubtful cases. It depends upon the fact that the addition of yeast to any urine which contains fermentable sugar produces a decomposition or fermentation, *i. e.*, the carbohydrates are transformed into alcohol and carbon dioxid gas. Proof of the fermentation is obtained by demonstrating the presence of the carbon dioxid. (Concerning the conclusions as to the type of carbohydrate, see p. 594 et seq.)

The fermentation test is performed as follows: A test-tube is filled to the brim with urine, a piece of ordinary compressed yeast [1] the size of a pea is dropped in, and the tube is then gently shaken until the yeast is finely divided, without allowing any air to enter. The tube is closed with a perforated cork which carries a V-shaped piece of glass tubing (Fig. 237, *b*). The test-tube is then inverted, placed in a beaker, and left in some moderately warm place (best, 25° to 30° C.). If the urine

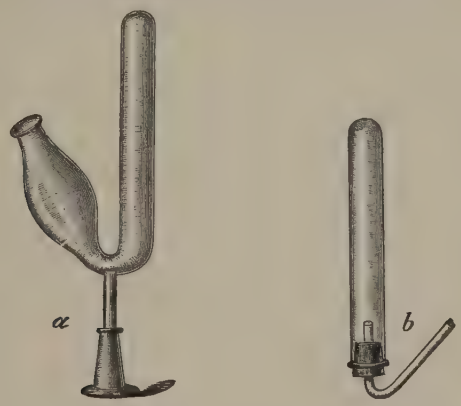


Fig. 237.—Apparatus for the qualitative test for sugar: *a*, Schrötter's fermentation tube; *b*, improvised apparatus.

contain glucose, carbon dioxid will be formed from it by fermentation inside of a few hours. The gas will accumulate at the upper end of the tube by expelling the urine through the V-shaped tube. Schrötter's gas tubes or fermentation tubes [2] are still more convenient (Fig. 237, *a*).

It is a good plan to prepare two other similar tubes, the one filled with normal urine and yeast, and the other with normal urine, yeast, and a knife-point of saccharose or glucose. These will serve to control any error which might arise, and to prove that the yeast is active. Provided it is performed with all the necessary precaution, the fermentation test is delicate enough to show $\frac{1}{10}$ to $\frac{1}{20}$ of 1 per cent. of sugar in the urine.

[1] The yeast may be washed with water, and the washings tested for glucose by Trommer's test. Yeast containing sugar must be thoroughly freed from glucose by washing. The compressed yeast of commerce is usually free from sugar. The Swiss pharmacopœia specifies a sugar-free yeast to be used in testing for glucose.

[2] Einhorn's tubes are very serviceable in this connection.

The first of the two control tests is absolutely necessary. The author has repeatedly observed that compressed yeast often develops gas in perfectly normal urine. This is due partly to the so-called "self-fermentation" of the yeast, which bears some relation to the amount of contained glycogen, and partly to a presumed bacterial contamination, which very quickly produces an ammoniacal fermentation of the urine and a consequent development of carbonic acid (from the ammonium carbonate derived from the urea. In this fermentation, however, the gas is not formed so quickly as in the fermentation of sugar, and it should consequently be required, not only that the formation of gas be considerable, but that it occur within a few hours and be unaccompanied by the signs of ammoniacal fermentation. This ammoniacal fermentation may always be suppressed by adding enough tartaric acid to make the urine decidedly acid in reaction.

Another precaution is to avoid shaking the urine too much when mixing it with the yeast, for in that case the liquid may absorb a considerable quantity of air, which afterward, upon standing, accumulates over the urine and may lead to error.

Test by Evaporation and Carbonization

The author believes that a very simple and rather sensitive test for sugar is to evaporate a drop of urine in a porcelain dish and then heat it a little more over a gentle flame. If any considerable quantity of sugar is present, the residue will be colored a pure yellow brown, even when the urine is much diluted; an odor of caramel can be appreciated before it is reduced entirely to ash, and if touched with a moistened finger, the residue will feel excessively sticky. Urine free from sugar will exhibit only a dirty-grayish-brown residue.

OCCURRENCE AND DETECTION OF OTHER FORMS OF CARBOHYDRATES AND DIFFERENTIATION OF GLUCOSE FROM THEM (Fructose (Levulose); Maltose; Isomaltose; Lactose; Pentoses)

Strictly speaking, the fermentation test only proves the presence of a fermentable sugar in the urine; or, in other words, it merely demonstrates the presence of some carbohydrate. Now, besides glucose, other types of fermentable sugars do occur in the urine; for instance, *fructose* and *maltose*. Thus far these have nearly always been observed in urine which also contains glucose, and they, therefore, do not materially influence the value of the fermentation test in the recognition of diabetes mellitus and of glycosuria. In addition to maltose, isomaltose (which is incapable of fermentation) has also been found in urine containing glucose (see below). It is also important to determine whether or not lactose (milk-sugar), which is not fermentable, is present; and so too the pentoses. Other important points of differentiation between the various carbohydrates which occur in the urine are the varying polarimetric properties of their solutions, especially as compared with their reducing power, and, further, the more or less characteristic osazones, which are formed in the phenylhydrazin test (p. 591 et seq.), and more especially the melting-point of the osazones. More accurate particulars upon this point will be found in text-books of chemistry. *Maltose* and *isomaltose* can be surely recognized and only by the demonstration of their osazones. Maltose and isomaltose are dextrorotatory and reduce an alkaline solution of copper. Maltose is fermented by yeast; isomaltose is not.

Lactose or milk-sugar, which is found in the urine of nursing women, after an exclusive milk diet with large quantities of milk, or after the ingestion of at least 100 gm. of lactose, does not ferment with ordinary yeast, but responds to Trommer's test. According to Malfatti, lactose may be detected by mixing the urine with half its volume of concentrated ammonia and heating the mixture in a hot-water bath not quite boiling. In from five to fifteen minutes the mixture becomes red; with glucose the color is yellow to brown. The author has had no experience with the test.

When urines contain both glucose and fructose, the polarimetric estimation of sugar gives a smaller value than that obtained by titration. This points to the presence of a levorotatory substance. When the urine is fermented, all rotatory power disappears. This would not be the case if the urine contained other levorotatory substances, such as cystin, β-oxybutyric acid, albumin, and paired glycuronic acids, which are not affected by fermentation.

In order to detect the presence of fructose, Seliwanoff's reaction may be used. To the urine is added an equal volume of concentrated hydrochloric acid containing resorcin in the following proportion: 0.5 resorcin, 30 cc. water, and 30 cc. concentrated hydrochloric acid. If a Burgundy-red color occur after heating, the presence of fructose may be suspected. The test is not, however, perfectly convincing.[1] Rosin[2] has suggested that the color be extracted with amyl alcohol after neutralizing the urine with sodium carbonate, and the alcoholic solution examined spectroscopically. Dilute solutions give an absorption-band in the green region of the spectrum between the lines E and B. More concentrated solutions show a second line in the blue at F. The color may be extracted from the alcohol by repeated shaking with water. The alcohol then becomes yellow in color. The red color in Seliwanoff's reaction must appear at once, for on continued heating other carbohydrates give the same reaction. Fructose may be formed from glucose in this way. According to Guiart and Grimbert, the formation of a precipitate soluble in alcohol after cooling is characteristic for the presence of fructose.

If the urine contain β-oxybutyric acid, besides glucose and fructose, the detection of the three is more complicated. The polarimetric and titration estimations do not agree, and after fermentation the urine is still levorotatory. The levorotation after fermentation is not sufficient to account for the difference between the results obtained by polarization and the estimation by titration.

The presence of paired glycuronic acids in the urine which not infrequently occurs in diabetic urines, and which also rotate the plane of polarized light to the left, may further complicate matters. Compare the detection of glycuronic acids, p. 597.

According to Strauss and Raspide, alimentary fructosuria is an important diagnostic sign of disease of the liver. Raspide (Thesis, Toulouse, 1903) found in 92 per cent. of cases of disease of the liver an alimentary fructosuria when the fasting patient was given 60 gm. of fructose in 200 cc. of water. The results are, however, complicated by the fact that in purely functional affections of the liver one obtains an alimentary fructosuria. The excretion of fructose may be detected one to three hours after its ingestion.

Presence and Detection of the Pentoses.—Pentoses are carbohydrates, each molecule of which contains 5 atoms of carbon, or some multiple of five. They have been found repeatedly in diabetic urine, but frequently also in urine without glucose.[3]

Pentosuria was first observed temporarily as so-called alimentary pentosuria after the ingestion of large quantities of fruits which are rich in pentoses, such as cherries, plums, huckleberries, and also after beer. In other cases, on the contrary, the elimination of pentose is chronic and independent of the quantity and nature of the pentoses in the ingested food. In these cases there is a specific pentose which is recognized by Neuberg as optically inactive arabinose. The amount of pentose in the urine may vary between 0.1 and 1 per cent., so that the daily quantity excreted can never exceed 20 gm. A theory for this pentosuria is still quite impossible. But pentosuria certainly bears no relation to diabetes mellitus. Bial[4] has also described pentosuria as a hereditary anomaly. The demonstration of pentose in the urine is clinically important only because an erroneous diagnosis of diabetes mellitus may be made. This is all the more important since it has repeatedly been observed that patients with pentosuria are injured by a rigid diabetic diet which does not influence the amount of excreted pentose in the slightest degree. Urines containing pentoses give a reduction with Trommer's and Nylander's tests.[5] They are optically inactive, and do not ferment with yeast. They show the following reaction:

Tollen's reaction is commonly employed for the detection of pentoses. Salkowski describes it as follows: A little phloroglucin is heated in 5 to 6 cc. of fuming hydrochloric acid, care being taken to leave a slight excess undissolved; the solution is divided into approximately equal parts. To 1 portion ½ cc. of the urine to be examined is added; to the other portion ½ cc. of normal urine. Both specimens are then warmed over a water-bath. It is advisable to decolorize both specimens

[1] F. Müller, Deut. Arch. f. klin. Med., 1904. Glucosamin gives the test.

[2] Zeit. physiol. Chem., xxxviii, 555, 556.

[3] Salkowski and Jastrowitz, Centralbl. f. d. med. Wiss., 1892, vol. xix; Salkowski, ibid., vol. xxxii, or Berlin. klin. Woch., 1895, No. 17; compare the collected account of Pentosuria by G. Bendix, Stuttgart, 1904; Bial, Berlin. klin. Woch., 1904, No. 21.

[4] Berlin. klin. Woch., 1904, No. 21.

[5] The reduction ordinarily occurs only after prolonged heating, and then quite suddenly throughout the entire solution.

of urine by heating with animal charcoal and filtering. If the urine contain pentose, an intense red zone will in a few moments appear at the top and gradually spread downward through the fluid. The control urine will not show any marked change of color. The tubes should be removed from the water-bath as soon as the color has developed distinctly, because if they are heated too long, the clearness of the reaction is interfered with. The red coloring-matter which appears in the reaction can be extracted with amyl alcohol, and will then show spectroscopically an absorption-band between the Fraunhofer lines D and E, *i. e.*, between yellow and green.

Even normal urine will sometimes furnish a doubtful coloration in this phloroglucin reaction. In such an event Salkowski recommends the *orcin test* employed by Reichel.[1] The urine is heated for twenty to thirty seconds with an equal volume of concentrated hydrochloric acid and a few particles of orcin. If the urine contains pentoses, a dark-green color appears; this is due to the formation of furfurol as the result of the boiling of urine containing pentose with HCl. The only other substance which gives the same reaction is glycuronic acid. This occurs, however, in the urine only in combinations which cannot be split up with such a brief boiling with HCl. Practically, therefore, we need not consider glycuronic acid when performing this test.

A dark-green precipitate gradually forms in the dark-green solution. This precipitate may be dissolved in amyl alcohol, producing a beautiful dark bluish-green color. The spectroscopic examination of this solution shows a characteristic absorption-band between C and D, *i. e.*, between red and yellow.

Bial[2] has recently recommended the following procedure for the practical demonstration of pentoses in the physician's office. He believes it to be sufficiently accurate to differentiate confusing cases of pentosuria from those of glycosuria. His reagent consists of 500 cc. of 30 per cent. hydrochloric acid, 1 gm. of orcin, and 25 drops of the official liquor ferri sesquichlorati (German Pharmacopeia). Four to 5 cc. of this reagent are boiled in a test-tube, and, after removal from the flame, several drops or, at most, 1 cc. of urine are added. A green color should appear at once or almost immediately. If the test be carried out in this manner, Bial states that the small amount of heat employed is not sufficient to cause any reaction between the reagent and the more unstable glycuronates. Moreover, Bial recommends the procedure, not for the differentiation of pentoses and combined glycuronates, but for the differentiation of pentosuria from glycosuria. It should, however, be remembered that both pentose and glucose may occur together in diabetic urine. A. Jolles[3] does not believe that Bial's test differentiates between glycuronic acid and pentoses, and suggests the following process: 10 to 20 cc. of the urine are treated with sodium acetate and phenylhydrazin hydrochlorid, as in the test for glucose. The precipitate is filtered through an asbestos filter, washed once with cold water, and the filter and its contents distilled from a flask containing 20 cc. of water and 5 cc. of concentrated hydrochloric acid. Five cc. are distilled over into 5 cc. of water. In the presence of pentoses Bial's reagent gives a marked green color. Neither glucose nor glycuronic acid gives this reaction. Practically one may confine Jolles' test to those urines which give Bial's test after fermentation.

The urinary pentoses may be further identified by the preparation of their osazones, which is accomplished by Salkowski as follows: In a beaker of about 400 cc. capacity are placed 5 gm. of phenylhydrazin, the same quantity of 50 per cent. acetic acid, and 200 cc. of urine. The mixture is well shaken, gently heated upon a piece of wire gauze, and then in a boiling water-bath, but not to boiling. The fluid is then filtered while hot, and cooled by placing the vessel in cold water; the crystals of pentosazone are then collected upon a filter, and purified by repeated recrystallizations with hot water. The final pure product is a golden-yellow powder, and, if pentoses were present in the urine, should have a melting-point of 156° to 160° C. (166°–168° C., according to Späth).

Cammidge's Reaction

Cammidge's reaction must be mentioned in this place. According to this observer, if the urines of patients suffering from disease of the pancreas be heated with hydrochloric acid, neutralized and acted upon with phenylhydrazin, an osazone is formed. It is assumed that the urine contains an unknown substance which splits

[1] Cf. Blumenthal, Zeit. f klin. Med., vol. xxxvii; Bial, ibid., vol. xxxix.
[2] Deut. med. Woch., 1903, No. 27.
[3] Centralbl. f. inn. Med., 1905, No. 43; 1907, No. 17.

off a pentose. The results of investigators of this reaction are not in agreement regarding its diagnostic importance in diseases of the pancreas. (See Eichler, Berlin. klin. Woch., June 24, 1907; Elösser, Grenzgebiete der Med. und Chir., 1907, vol. xviii.

DETECTION OF GLYCURONIC ACID

Glycuronic acid is formed in the body, probably even under physiologic conditions, by the oxidation of glucose, from which it differs but little in its elementary composition. It appears in the urine when an opportunity is furnished for it to become combined in the organism with other bodies, and so to escape complete oxidation. There are a great many substances which may combine with glycuronic acid. Among them are chloral hydrate, morphin, camphor, oil of turpentine, salicylic acid, saccharin, santonin, thallin, chrysophanic acid, menthol, most of the phenols and phenol derivatives, *i. e.*, indol, skatol, naphthol, etc. Flückiger[1] has proved that, aside from the uric acid and kreatinin contained, the reducing power of normal urine depends upon the presence of the paired combinations of glycuronic acid, especially the phenol, parakresol, indol, and skatol glycuronates. P. Mayer[2] has more recently confirmed these observations, and in addition has shown that the excretion of the combined glycuronates has a bearing upon diabetes mellitus and upon alimentary glycosuria. He claims that after excessive ingestion of carbohydrates, and especially of glucose, large quantities of the glycuronic acid salts are sometimes excreted in human urine before sugar appears. In these cases it seems as if the organism were able to oxidize the ingested sugar up to the stage of glycuronic acid, but no further. This hypothesis of the origin of glycuronic acid will explain the frequently coincident occurrence of combined glycuronates and glucose in the urine which has been observed both in alimentary glycosuria and in diabetes mellitus. Here a part of the glucose which is not utilized has been oxidized only to glycuronic acid. Glycuronic acid is capable of reducing, but not of fermenting. This explains the peculiarity which has been observed in the urine of a diabetic patient upon a successful diet, *i. e.*, it still reduces but does not ferment. Even the reduction is peculiar in that, unlike the glucose reduction, it occurs very slowly (see below). Many discrepancies between the quantitative estimations of the amount of sugar by the polarization, by the fermentation, and by the copper tests can thus be explained by the simultaneous presence of glucose and some combined glycuronates. The latter, unlike the sugar, rotate to the left, but like it, reduce. Glycuronic acid has never been found in the urine except in combination. P. Mayer claims that these combinations can be split up by boiling for one to five minutes with 1 per cent. H_2SO_4, and that the peculiarities of the combined and of the artificially separated glycuronic acid can be examined in the urine. The duration of the boiling must be determined in the case of each combined glycuronate by demonstrating that the urine has changed its character in the maximum manner expected. No definite time can be given for all cases.

The following are the reactions usually employed to detect the combined glycuronates in the urine:

1. The urine reduces an alkaline solution of copper. Since the combined glycuronates reduce but slowly, this reduction occurs only after prolonged heating. It will, on the contrary, take place immediately if we boil the urine beforehand, by the method mentioned above, with 1 per cent. H_2SO_4, in order to cause the cleavage of the glycuronate combinations.

2. The free acid, but not the combined glycuronates, will enter into combination with phenylhydrazin. Hence, the phenylhydrazin test, employed for demonstrating the presence of sugar (p. 591 et seq.), will give a negative result if we employ the ordinary urine containing the combined glycuronates; but, on the contrary, it will furnish a positive result if we precede the test by first boiling the urine with 1 per cent. H_2SO_4.

3. Glycuronic acid does not ferment, but it does reduce alkaline copper solutions; therefore, a urine containing glycuronates, in spite of its reducing power, does not ferment. If sugar be also present, fermentation will produce an incomplete loss of the power of reduction.

4. The free glycuronic acid is dextrorotatory, while the combined glycuronates rotate to the left. With urine containing compounds of glycuronic acid this levogyrate power will be changed to dextrorotation after boiling with H_2SO_4 (see above).

[1] Zeit. f. physiol. Chem., 1885, No. 9.

[2] Berlin. klin. Woch., 1899, p. 617 et seq., and Deut. med. Woch., 1901, No. 16 and 17.

Again, if there is also glucose in the urine, the dextrorotatory power will be increased after boiling.

5. Tollen's reaction (see p. 595 et seq.) is positive with urine containing glycuronic acid as with urine containing pentoses, but not if glucose be present alone. (See Pentoses.)

6. Urine containing glycuronates reacts to the orcin test only after cleavage of the combination has occurred by boiling with 1 per cent. H_2SO_4. This is in contrast to urine containing pentoses (p. 595).

DETECTION OF ACETONE (CH_3—CO—CH_3)

Traces of acetone occur in every normal urine. The amount will be increased in fever, with starvation, with a purely meat diet, in diabetes mellitus, in certain forms of digestive disturbances, and in some cases of carcinoma.

Recent investigations have shown that the cause of the increased acetone elimination is to be found in the removal of carbohydrates from the diet, so that the energy requirements of the body are supplied by proteins and fats. A healthy individual may eliminate considerable quantities of acetone if carbohydrates be removed from the food. In diabetes mellitus the conditions are similar, for the organism is unable to properly combust carbohydrates. In less severe cases where there is a partial tolerance for carbohydrates acetonuria occurs only where, through dietary regulation, the carbohydrates have been more or less restricted. In the more severe cases in which the combustion of carbohydrate is distinctly reduced, one finds an increased elimination of acetone with a diet containing carbohydrates, for in spite of the administration of these substances, the capacity for their combustion is practically lost. The increase in the acetone content of the urine is, therefore, an important criterion as to the use which a diabetic is making of a given diet, and, therefore, of the severity of the diabetes itself. It must be remembered that in so-called carbohydrate-free diets the carbohydrates split off from proteins in the course of metabolism are used as the free carbohydrates themselves. A similar explanation holds for other conditions associated with acetonuria as it does for diabetes. The idea of a special acetonuria or acetonemia does not obtain to-day. The conditions necessary for the increased elimination of acetone in all these cases is a decreased or inhibited carbohydrate combustion. With regard to the source of the acetone compounds, it is generally assumed that the fats, which with incomplete carbohydrate combustions are katabolized abnormally, furnish the greater part of the acetone compounds, while the proteins play a secondary rôle, mainly through the amino-acids into which they are at first broken down. In spite of this assumption, an increase in the amount of fat administered does not increase the elimination of the compounds, with certain exceptions.[1]

This is due to the fact that the fat metabolism is only indirectly contingent on the amount of fat administered, as the ingested fat is first stored up in the tissues, and is from there slowly utilized. Acetone is probably formed from aceto-acetic acid, and this from β-oxybutyric acid. The last is the product of the abnormal fat metabolism. Acetone, aceto-acetic acid, and β-oxybutyric acid stand in close genetic relationship, and all are grouped together under the term acetone compounds, or acidosis compounds.

[1] Stäubli, Deut. Arch. f. klin. Med., 1908, vol. xciii.

An excellent résumé of the whole subject will be found in the article by Magnus-Levy, in the Ergebnisse der inneren Medizin und Kinderheilkunde, 1908, Springer, Berlin; also Ewing, Arch. Int. Med., 1909.

By acetonuria in the clinical sense is understood an increased elimination of acetone in the urine, which may be suspected from the fruity odor which the urine possesses, and also by the sweetish odor of the breath. Magnus-Levy believes that the greater part of the acetone does not occur preformed in the urine, but is the result of the breaking down of aceto-acetic acid while testing for acetone.

The test for acetone can first be tried with the urine itself. If the result is negative, the urine should be distilled. Acetone is very volatile, so that the distillate will be much richer in acetone than the urine, and smaller quantities can thus be detected.

Distillation can be performed without any complicated apparatus in the following way: About 50 cc. of urine acidified with a little phosphoric acid (sufficient for a marked Congo reaction, to prevent foaming) are poured into a fractionation flask (Fig. 238) and heated to gentle boiling, preferably over a water-bath or over a wire gauze. A test-tube is then slipped over the projecting neck for a receiver and fastened with a piece of string or wire. The upper, open end of the flask is closed with a cork. The distillate will now collect in the test-tube without any special cooling apparatus. Within a few minutes several cubic centimeters will have distilled over, and the acetone test can then be performed upon the distillate.

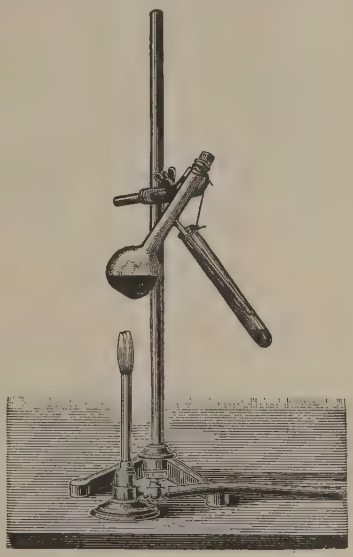


Fig. 238.—Fractionation flask.

Hoppe-Seyler claims that if acetoacetic acid be also present, the distillation will produce acetone artificially, so that in such an event another method must be selected. Instead of being distilled, the urine is rendered slightly alkaline and then extracted with pure ether, the ether shaken with water, and the test performed upon the aqueous solution.

To demonstrate the presence of acetone, one of the following tests is usually employed:

Gunning's Iodoform Test.—A little Lugol's solution[1] is added to the distillate, and then enough ammonia to produce an intense black precipitate of nitrogen iodid. This precipitate will gradually disappear upon standing, and when acetone is present, a yellowish sediment consisting of iodoform will take its place. It can be recognized by its

[1] Composition of Lugol's solution: 1.2 gm. iodin, 1.8 gm. potassium iodid, 30 parts of water. Instead of Lugol's solution and ammonia, one may use tincture of iodin and ammonia, or a solution of iodin in ammonium iodid (1 part iodin, 2 parts of ammonium iodid, and 30 parts of water).

odor or microscopically, as it consists of hexagonal plates or small stars (compare Fig. 239); occasionally the precipitate is amorphous. We must be careful not to confound with the iodoform crystals the stellate crystalline aggregations of triple phosphate which are often produced along with them, especially where the urine itself, instead of the distillate, is employed. (This is also possible with Lieben's test, see below.) (See Fig. 257.) If the urine contain but a small amount of acetone, it may be necessary to wait twenty-four hours before the iodoform crystals can be demonstrated. If the crystals are not distinctly formed, they may be recrystallized for more certain recognition, first dissolving them in ether and then allowing this to evaporate slowly. Gunning's test has a great advantage over Lieben's (see below), because with it no other known substance, and especially neither alcohol nor aldehyd, will produce iodoform. On the other hand, it is somewhat less delicate than Lieben's. But even so, it is extremely delicate, and often readily permits the detection of acetone in diabetic urine without distillation. The author recommends Gunning's test first of

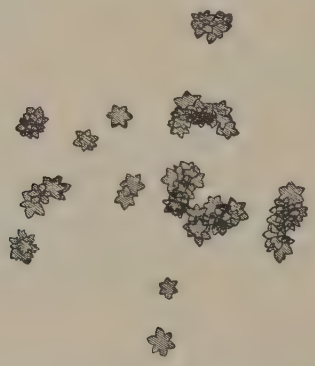


Fig. 239.—Iodoform crystals from the precipitate in Gunning's test (after a microphotograph).

all for clinical use, and particularly when it is desirable to demonstrate acetone in the urine directly without distillation.

Lieben's Iodoform Test.—Some potassium hydroxid and Lugol's solution are added to the urine, or better to its distillate. If acetone be present, a yellowish precipitate will be formed, and will be recognized, as in Gunning's test (see above), by its odor and by the shape of the crystals. If only a very small amount of acetone be present, the iodoform precipitation may be delayed some hours, even up to twenty-four. This test is extremely delicate, but it is less distinctive than Gunning's, because with it other substances besides acetone may give rise to iodoform (alcohol, for example); Gunning's test is therefore preferable.

Legal's Test.—Three drops of a freshly prepared concentrated solution of sodium nitroprussid (1 : 10) are added to the urine itself, or better to its distillate, and the mixture made strongly alkaline with a few drops of sodium or potassium hydroxid. The red color which arises gradually changes to yellow. This color reaction depends upon the presence of kreatinin, and will be seen in every urine. But if any considerable amount of acetone be contained in the urine, the addition of

acetic acid will discharge the yellow color, and the solution will become purple red or violet. This test may lead to the erroneous supposition of the presence of acetone if the urine contain parakresol (von Jaksch). It is the one which is usually recommended for the direct examination of urine without distillation; but, according to the author's experience, it is not in that case very delicate, and he does not recommend it. If the distillate be used, however, the test is a useful one, and has recently been recommended by Studer.

In order to avoid confusion with aldehyd, Le Noble and Lee suggest the use of ammonia instead of potassium or sodium hydroxids.

Lange's Test.—Lange[1] suggests a ring test as a modification of Legal and Le Noble's tests, and which appears to be more delicate. Fifteen cc. of the urine are mixed with 0.5 to 1.0 cc. of acetic acid, and a few drops of a freshly prepared concentrated solution of sodium nitroprussid added. The mixture is overlaid with ammonia. At the point of junction, a characteristic intense violet ring is formed. The color appears gradually and spreads in the course of time through the mixture.

DETECTION OF ACETOACETIC ACID (DIACETIC ACID) ($CH_3.COCH_2.COOH$)

Acetoacetic acid does not occur in the urine of healthy individuals upon an ordinary diet, except, perhaps, in very small quantities. As Magnus-Levy has pointed out, most of the acetone found in the urine is in the form of acetoacetic acid, and hence the acid is to be observed in the same class of cases as acetone itself: in fasting, in diabetes mellitus, strict meat diet, fever, dyspeptic conditions, etc. It is usually possible to detect acetone simultaneously with acetoacetic acid in the urine. If little acetoacetic acid be formed, it is all transformed into acetone; if much, then both substances will be found in the urine. It frequently happens that the mother substance of diacetic acid, β-oxybutyric acid, is also present. Diaceturia, like acetonuria, also bears some relation to the metabolism of the carbohydrates, since in the diaceturia of non-diabetic individuals the proteins are decomposed without the simultaneous oxidation of the carbohydrates, and it may frequently be suppressed by the administration of carbohydrates. The excretion of a large amount of acetoacetic acid by a diabetic upon a mixed diet, like the excretion of acetone under the same circumstances, is an indication of a severe form of the disease. Such diaceturia is favored by a rigid meat diet, and may frequently be diminished by the ingestion of carbohydrates. It would be just as erroneous to assume that diaceturia has a definite symptomatology as it would be to state that acetonuria is a distinct clinical entity. It should also be noted that the appearance of acetoacetic acid in the urine is usually accompanied by an increased elimination of ammonia, as is also the excretion of β-oxybutyric acid.

According to Stäubli (see p. 653), the amount of acetoacetic acid and acetone is not always parallel to the amount of β-oxybutyric acid in the urine. A strong reaction for acetoacetic acid does not always indicate a high grade of acidosis. This must be remembered when forming a prognosis, and in regulating the diet in diabetes mellitus.

The presence of acetoacetic acid can be demonstrated as follows:

Gerhardt's Diabetic Ferric Chlorid Reaction.—One or two drops of a ferric chlorid solution are added to the urine. If diacetic

[1] Münch. med. Woch., 1906, No. 36.

acid be present, a Bordeaux-red color appears, which is most distinct after filtering off the precipitate of ferric phosphate. If an insufficient quantity of the ferric chlorid solution has been added, an extra amount must be employed after the phosphate precipitate has been removed by filtration. Thiocyanates, sodium acetate, salicylic acid, antipyrin, thallin, kairin, and other aromatic substances may produce a similar red color. For this reason the presence of acetoacetic acid should be assumed only after positive results have been obtained by the two following control tests:

1. If boiled urine be employed for the test, the red color should be very much fainter, because boiling gradually transforms aceto-acetic acid into acetone. 2. The urine is acidified with sulphuric acid and then shaken with ether. Acetoacetic acid, if present, will be taken up by the ether, and, if the latter be shaken with a diluted solution of ferric chlorid, the aqueous layer will turn red. The coloring will disappear spontaneously in twenty-four to forty-eight hours. The sulphuric acid merely serves to free the acetoacetic acid from its salts, so that it may be taken up by the ether. Thiocyanates react similarly in this control test, because thiocyanic acid also dissolves in the ether. In that case, however, the red color does not disappear spontaneously. The color produced by sodium acetate, salicylic acid, antipyrin, thallin, and kairin also remains permanent for days.

As the test is not a very delicate one, and is interfered with by phosphates, Kaliski has suggested that the urine be made strongly acid with sulphuric acid and extracted with ether. A few drops of a dilute ferric chlorid solution are added to the ethereal extract. At the junction of the aqueous and ethereal layers a deep red ring is formed.

Arnold-Lipliawski Test for Acetoacetic Acid.—This test is said to be more delicate than that of Gerhardt, and does not give rise to the same complications. The solutions necessary for the test are: (1) Para-amidoacetophenone, 1 gm.; concentrated hydrochloric acid, 2 cc., dissolved in 100 cc. of water. (2) Potassium or sodium nitrite solution, 1 per cent. Six cc. of the first and 3 cc. of the second are mixed together, an equal volume of the urine added, and 1 drop of ammonia. A bright red color is produced. According to the amount of acetoacetic acid present in the urine, 0.5 to 2 cc. are taken, and 10 to 20 cc. of hydrochloric acid, 2 cc. of chloroform, and 2 to 4 drops of ferric chlorid added. In the presence of aceto-acetic acid the chloroform is colored violet; otherwise, the color of the chloroform becomes yellow. The reaction only takes place by using concentrated hydrochloric acid with a specific gravity of 1.19.

DETECTION OF β-OXYBUTYRIC ACID

β-oxybutyric acid does not appear to be present in normal urine (Magnus-Levy). Its presence is associated with the same anomalies of metabolism as are acetone and aceto-acetic acid. (See p. 598.) It is found in fasting and in strict protein diets, in diabetes mellitus, in fever, and in disturbances of digestion which are associated with decreased utilization of carbohydrates. The mother substances of β-oxybutyric acid are the fats and the proteins. The theoretic questions concerning the formation of the acid are discussed in detail in Magnus-Levy's article, Ergebnisse der inneren Medizin und Kinderheilkunde, Springer, Berlin, 1908.

In diabetes mellitus a considerable amount of β-oxybutyric acid in the urine suggests the onset of acid intoxication or "acidosis" (coma diabeticum).

β-oxybutyric acid appears to be present in the urine only when diacetic acid is there also (see above).

Unfortunately, the process for demonstrating β-oxybutyric acid is very complicated. The acid must first be isolated, and then a well-characterized salt of oxybutyric acid be formed.[1] This acid is levogyrate, while glucose is dextrogyrate.

[1] For a detailed description see Minkowski, Arch. f. exp. Path., 1884, vol. xviii and xxi, and Külz, ibid., or Külz, Zeit. f. Biol., vol. xx and xxiii.

In some cases of diabetes mellitus we may, therefore, suspect the presence of β-oxybutyric acid if the amount of glucose, as determined by titration, is distinctly larger than that obtained by the polariscope. Protein must, of course, be absent, as that, as well as β-oxybutyric acid, is levogyrate. Levulose may lead to confusion.

E. Külz first removes the protein from the diabetic urine, next the sugar by fermentation (which will also dispose of the levulose), then decolorizes by precipitating with lead acetate and ammonia, and finally examines with the polariscope. If after this process the urine still exhibits a tendency to left-handed rotation, β-oxybutyric acid is in all probability present. To be certain we must exclude the presence of combined glycuronates. The latter condition must also be fulfilled if we are to assume the presence of β-oxybutyric acid from the left-handed rotation of the ethereal extract obtained from the fermented urine which has been strongly acidulated with phosphoric acid.

Waldvogel's Test.—Three hundred cc. of the suspected urine are evaporated to 100 cc. A similar test is made with a normal urine. To each evaporated urine are added 10 cc. of 10 per cent. sodium hydroxid solution. Both are very vigorously stirred with a glass rod. Normal urine does not froth, while a specimen containing β-oxybutyric acid gives a distinct soapy foam. This test only indicates the probable presence of β-oxybutyric acid in the urine.

An almost positive proof of the presence of β-oxybutyric acid in cases of diabetes mellitus is the detection of acidosis, as shown by a considerable increase in the quantity of ammonia excreted in the urine. (See p. 651.)

[A distinct advance has been made in the last two years in the methods used for the determination of acetone, acetoacetic acid, and β-oxybutyric acid through the investigations of Folin and of Shaffer.[1] The methods, which are complementary to one another, depend upon the facts that—(1) acetone is removed completely from the urine by a current of air if the urine be saturated with sodium chlorid; (2) acetoacetic acid is completely converted into acetone by heating with acids; and (3) β-oxybutyric acid is converted into acetone by treatment with an oxidizing agent. The one employed is potassium bichromate and sulphuric acid.

If one removes successively the acetone due to preformed acetone and acetoacetic acid, and oxidizes the residue, one may obtain the acetone formed from β-oxybutyric acid. The analytic procedure is much less complicated than those of previous methods, and gives more accurate results. We are now in a position to study problems of acidosis with methods which lend themselves to routine use.

The methods are as follows:

Acetone.—Folin's Method.—The same apparatus is used in this method as is described in Folin's method for ammonia. The procedure is as follows: 25 cc. of the urine to be examined are introduced into a cylinder, and 10 drops of phosphoric acid, 10 per cent., and 8 to 10 gm. of sodium chlorid, and a little kerosene to prevent frothing. Into the absorption flask are placed 150 cc. of water, 10 cc. of potassium hydroxid, 40 per cent., and a measured volume of decinormal iodin solution. The absorption flask is connected with the areometer cylinder and a current of air drawn through the system. Suction is continued for twenty to twenty-five minutes. All of the acetone is carried over by the air into the absorption flask and is converted into iodoform by the alkaline hypoiodite. Ten cc. of concentrated hydrochloric acid are added. If the amount of iodin used has been in excess of the amount required by the acetone for conversion, the original brown iodin color will be produced. The excess of iodin is titrated with decinormal sodium thiosulphate, using a solution of starch as an indicator. Every cubic centimeter of decinormal iodin solution which has been absorbed by the acetone represents 0.96 mg. of acetone.

Acetoacetic Acid.—This may be determined by Hart's modification of Folin's method. The same apparatus as was used in the foregoing test may be employed. After the preformed acetone has been removed from the urine, the urine is heated nearly to boiling by immersing the cylinder in a water-bath, another absorption apparatus being employed, charged with fresh iodin solution. The current of air is

[1] For a discussion of the question concerned in acidosis see Ewing, Arch. Internal Medicine, 1908, ii, p. 485.

run for twenty-five minutes, during which time all acetoacetic acid is converted into acetone and carried over with the air-current. This amount of acetone represents that due to acetoacetic acid.

β-Oxybutyric Acid.—Shaffer's Method.—Introduce into a 500-cc. flask 25 to 250 cc. of the urine to be examined. The amount employed depends upon the amount of β-oxybutyric acid the urine is suspected to contain. In the case of urines giving a strong ferric chlorid reaction it is unnecessary to use more than 25 to 50 cc. It is desirable to use an amount of the urine which will give 25 to 50 mg. of acetone. An excess of basic lead acetate is added to the urine and 10 cc. of concentrated ammonium hydroxid. One must ascertain that an excess of the acetate is present. On filtering, a few drops of the reagent should give no further precipitation. The contents of the flask are diluted to 500 cc. and shaken. The mixture is filtered. Transfer 200 cc. of the filtrate to an 800-cc. flask, add 300 to 400 cc. of water, 15 cc. of concentrated sulphuric acid and a little talcum powder, and distil the mixture until 250 cc. have passed over. This distillate contains the acetone from the preformed acetone and acetoacetic acid in the urine, and may be used for its determination. The residue from which the distillate was obtained is redistilled after adding about 500 cc. of water and 0.5 gm. of potassium bichromate. During this distillation water is added to the residue by means of a funnel tube placed in the neck of the flask, so that the liquid distilled over is replaced by water and the volume of liquid in the flask kept constant. Under no circumstance may the liquid in the flask assume a green color, showing that the potassium bichromate has been entirely used up. If this be the case, more bichromate must be added to the flask through the funnel tube. After about 500 cc. of distillate have passed over, the distillate is taken, about 20 cc. of hydrogen dioxid, 3 per cent., are added, and a few cubic centimeters of potassium hydroxid. This is now distilled, 300 cc. of distillate being collected. Twenty-five or 50 cc. of decinormal iodin solution are added to the distillate, and 10 cc. of a 40 per cent. solution of potassium hydroxid added. The mixture is shaken well and allowed to stand for five minutes. Ten cc. of concentrated hydrochloric acid are added, and the mixture titrated with decinormal iodin solution. The amount of iodin absorbed by the acetone present represents that due to the β-oxybutyric acid in the urine. Each cubic centimeter of iodin absorbed represents 1.794 mg. of β-oxybutyric acid.

The results in all these three methods of determination are accurate.—C. G. L. W.]

DETECTION OF ALKAPTON (HYDROCHINON ACETIC ACID OR HOMOGENTISIC ACID)

The substance which has been named *alkapton* lends to the urine the peculiar property of becoming extremely dark after standing for some time. The urine turns a dark to brownish-black color from oxidation, especially if it be alkaline in reaction. Urine stains upon the clothes are dark-red to brownish. Urine containing alkapton reacts positively to Trommer's test, but it can be distinguished from urine containing sugar by its negative reaction to Nylander's test and by its inability to ferment, and by the greenish tinge produced by the addition of a dilute solution of ferric chlorid. It is also optically inactive. This color will disappear promptly, but can be brought out again by the fresh addition of the reagent. With Millon's reagent,[1] a lemon-yellow precipitate is formed, which becomes red on warming.

The chemic nature of alkapton was for a long time unknown. Baumann and Wolkow's[2] investigations have, however, definitely placed the substance as a derivative of hydroquinon, and regard it as hydrochinon acetic acid or homogentisic acid. Only in one case were they able to demonstrate with it a related acid—hydrochinon lactic acid or uroleucinic acid. Alkaptonuria is, for the most part, unassociated with any discomfort, and has generally been demonstrated as a rare circumstance, occurring in an apparently healthy individual. In Stange's case it was associated with dysuria. The etiology of the condition is quite unknown. The amount of homogentisic acid appears to be quantitatively dependent on the amount of protein ingested. The subject is discussed by E. Meyer,[3] where the older literature is given, and also by Langstein and Meyer.[4] Both authors come to the conclusion that alkaptonuria is an anomaly of intermediary metabolism, in which the acid is formed from the protein of the food and also from the proteins katabolized in the func-

[1] Millon's reagent is made by dissolving 1 part of mercury in 1 part of fuming nitric acid (specific gravity, 1.42). The solution is diluted with 1 or 2 parts of water, and filtered after standing some hours.

[2] Zeit. f. physiol. Chem., vol. xv.

[3] Deut. Arch. f. klin. Med., vol. lxx.

[4] Ibid., 1903, vol. lxxviii.

tioning of the organs. A further review of the subject will be found in an article by Blum,[1] in which are discussed the views put forward by Albrecht, Zdarek, Osler, and more recently by A. Wagner, regarding the connection between alkaptonuria and the pigmentation of the joints which was called ochronosis by Virchow. L. Blum comes to the conclusion that, as in cystinuria, alkaptonuria is a disturbance of metabolism in which, in the former, the aliphatic groups of the protein molecule are involved, and in the latter, the aromatic. According to Embden, this takes place normally in the liver. Neubauer and Falta have shown that all aromatic compounds which are capable of combustion in the body increase the amount of alkapton in the alkaptonuric. This is not the case with normal individuals.

[The experimental relationship between alkaptonuria and ochronosis has been established by Gross and Allard,[2] who have shown that cartilage allowed to stand in a solution of homogentisic acid, the substance excreted in the urine in alkaptonuria, was stained deep black by the acid. Wagner[3] demonstrated postmortem that the cartilages of a case of alkaptonuria showed ochronosis.—C. G. L. W.]

DETECTION OF LEUCIN AND TYROSIN

Any appreciable quantity of leucin and tyrosin in the urine is always pathologic. They are nearly always in solution. Their presence is

Fig. 240.—Leucin spheres and plates and tyrosin needles in the urine of a case of acute yellow atrophy examined by Huppert's method; precipitation of urine with basic lead acetate, filtration, treatment of filtrate with hydrogen sulphid; evaporation, as far as possible, of filtrate; filtrate extracted with a little alcohol, alcohol poured off. Residue extracted with boiling ammoniacal alcohol, filtered, and filtrate allowed to stand over night. The needles are tyrosin, the plates and plain and radially striated spheres are leucin (Zeiss E, eye-piece I).

very characteristic of acute yellow atrophy of the liver and phosphorus-poisoning, and is found more rarely in typhus, variola, pernicious anemia, and leukemia.

[1] Semaine medicale, 1906, No. 47.
[2] Arch. f. exp. Path. u. Pharm., 1908, lix, p. 384.
[3] Zeit. f. klin. Med., 1908, lxxix, p. 179.

In order to detect them, the urine is first evaporated to about one-tenth its volume and a little alcohol then added. If the urine contain albumin, this must first be removed. The characteristic crystals of the two substances can then be recognized microscopically. Tyrosin crystallizes in the shape of needles; leucin, in spheres (Fig. 239). The latter can be differentiated from the crystals of ammonium urate (see Fig. 256) by their much sharper line of contour, their less refractive power, and their absence of prickles. Leucin and tyrosin are precipitated, as a rule, in icteric urine (acute yellow atrophy of the liver and phosphorus-poisoning). Hence we must not confound the tyrosin needles

Fig. 241.—Leucin spheres and plates and tyrosin needles from urine in acute yellow atrophy. Other forms than in Fig. 240, with other methods of preparation. The urine was evaporated to a syrup and alcohol added; the needle and sheaves are tyrosin; the spheres and granules are leucin (Leitz 5. Eye-piece I).

with bilirubin needles, which are sometimes precipitated (Fig. 278) by the concentration of the urine. The latter can usually be recognized by their intense brownish-red color.

Unless the crystals of leucin and tyrosin are very characteristic, it is always much safer to perform the following test (taken in part from Huppert): The urine is precipitated with basic lead acetate (liquor plumbi subacetatis). The filtrate is freed from the excess of lead with hydrogen sulphid, then evaporated as much as possible, the residue extracted with a small amount of absolute alcohol (to remove the urea), then the undissolved residue extracted with slightly ammoniacal alcohol. The extract is evaporated to a small volume and left to itself until leucin and tyrosin crystallize out. Leucin and tyrosin may now be separated by crystallization from water. The substance crystallizes first which saturates the solution first according to the amount and degree of solubility. By recrystallizing from the ammoniacal alcohol, both substances may be obtained fairly pure. The two substances may

be separated by recrystallization in a little alcohol, in which leucin is more soluble than tyrosin. Tyrosin gives a red color on heating with Millon's reagent. (See foot-note, p. 604.)

In a case of acute yellow atrophy in the author's clinic the following procedure suggested by Heffter was successfully employed. Two hundred cc. of urine were treated with basic lead acetate as long as a precipitate was formed with the reagent. The excess of lead was removed with hydrogen sulphid, the lead sulphid filtered off, and the solution evaporated to about one-third to one-fourth its original volume. On cooling, the tyrosin separated out and was filtered off. It responded to the Denigés-Mörner test. The leucin can be obtained by further evaporating the filtrate.

The pure tyrosin which is thus formed must react to *Piria's test.* This is performed by boiling the dry tyrosin in a dry test-tube with a few drops of sulphuric acid in a water-bath for one-half hour. The resulting reddish solution of tyrosin sulphuric acid is allowed to cool, and then poured into several times as much water, the test-tube rinsed with water, and the solution neutralized with barium carbonate. The mixture is then filtered and boiled down to a few cubic centimeters; when cool, some dilute neutral ferric chlorid is carefully added. A beautiful violet color results, quite like that of iron salicylate (p. 611). Besides this (according to Hoffmann) a hot aqueous solution of tyrosin, to which have been added potassium nitrate and mercuric nitrate, should produce a beautiful dark color and an abundant red precipitate so long as it is kept hot. Or, one performs Mörner's modification of Denigé's test. The reagent is made after mixture of 5 parts of commercial formalin (40 per cent.), 55 parts of concentrated sulphuric acid, and 4 parts of water. If a small quantity of tyrosin be heated with 1 cc. of this reagent, a green color is produced. Denigé heated a small amount of tyrosin with 2 or 3 drops of sulphuric acid and added a few drops of concentrated formalin; a red color was produced, which after the immediate addition of acetic acid turned green. These tests do not succeed well with the urine itself.

Leucin, on the other hand, when gently heated, is characterized by subliming without melting, and at the same time emitting an odor of amylamin. It can also be identified by *Scherer's test.* This is performed by evaporating leucin with nitric acid on a piece of platinum foil; sodium hydroxid is added to the cold residue and then warmed. When the resulting solution is concentrated, it contracts to an oily drop, which rolls around and does not adhere to the platinum. Salkowski also tries the following reaction: A sample of the substance, not too small, is dissolved in water, then decolorized, if necessary, with bone charcoal; the filtrate is made alkaline with NaOH, and 1 or 2 drops of copper sulphate solution (1: 10) added. The cupric hydroxid, which is first precipitated, dissolves, and a blue solution results from the formation of leucin-copper, which is not reduced on heating. Leucin crystals dissolve in solutions of caustic potash and are insoluble in ether. This serves to differentiate them from fat, with which they might be confused.

DIAZO-REACTION

Ehrlich[1] tried to discover unknown constituents of the urine by employing the diazo-compounds, which produce colored combinations with a large number of aromatic substances. The nature of the body which is found in certain pathologic urines, and which gives the so-called diazo-reaction, is still unknown. Späth claims that the reaction should be ascribed to oxyproteic (uroproteic) acid, a recently discovered[2] normal urinary constituent, in case the urine contain an increased quantity of this substance. The author cannot confirm this statement. According to Burian,[3] the diazo-reaction is due to an increase in the excretion of purin bases, and is, therefore, a sign of the increased katabolism of tissues containing nucleins.

The test is performed as follows: Two stock solutions are employed. (1) A 0.5 per cent. solution of sodium nitrite. (2) A solution of 5 gm. of sulphanilic acid in 50 cc. of hydrochloric acid and 1000 cc. of distilled

[1] Zeit. f. klin. Med., 1882, vol. v, p. 285.
[2] Almost simultaneously by Bondzynski and Gottlieb and by M. Cloetta.
[3] Ber. d. deut. Chem. Gesellschaft, 1904, vol. xxxvii.

water. Fifty cc. of the latter, freshly mixed for each test with 1 cc. of the former solution, make up the reagent. It may be prepared approximately in a test-tube, in the absence of a measuring-glass, by adding about to 3 cc. of solution No. 2 a drop of the nitrite solution (No. 1). Equal parts of urine and of the reagent are mixed and then quickly supersaturated with ammonia. The characteristic reaction now consists in the mixture turning more or less intensely red, the foam which forms upon shaking being tinged from a rose to deep red; the reaction is then positive. The brownish-yellow color which appears when the test is performed with any normal urine must not be mistaken for the characteristic rose-red coloration. When the test is positive and the mixture is allowed to stand, after some time a precipitate forms, whose upper margin exhibits a dark zone of a green or greenish-black or even violet shade. Any deviation from the above procedure will produce other results, and should, therefore, be avoided, *e. g.*, the supersaturation with ammonia must be done at once, and not drop by drop.

The author must add, however, that he has observed cases where the Ehrlich procedure has given a negative test, but where the addition of ammonia drop by drop, so that the urine was overlaid, has given a positive test. He, therefore, recommends in doubtful cases that the second method should also be used.

In the latter procedure the ammoniacal layer is colored, the point of junction of the two layers showing the deepest red.

So far as the clinical results are concerned, Ehrlich claims that the reaction is never found in healthy individuals, and only exceptionally in non-febrile diseases: 1, In advanced cardiac disease; 2, in chronic hepatitis; 3, in carcinoma, especially of the pylorus; 4, in leukemia; 5, in marasmus senilis; 6, in the cachexia of malaria; 7, in cold abscesses. So far as febrile affections are concerned, they may be divided into three subdivisions: 1, Those in which the reaction is almost always absent, *e. g.*, joint rheumatism, meningitis; according to Stäubli, the diazo-reaction is constant in severe cases of trichinosis; 2, those in which it may occur sometimes more often, sometimes less often, according to the nature of the attack, *e. g.*, pneumonia, scarlet fever, diphtheria, erysipelas, phthisis; 3, those in which it is of nearly constant occurrence, *e. g.*, typhoid, typhus, measles.

The occurrence of the reaction in either of the first two categories of febrile disorders appears to render the prognosis more grave.

In typhoid the reaction may be of diagnostic value in one of two ways: First, the persistent absence of this reaction in a disease which simulates a severe typhoid speaks, although not absolutely, against such diagnosis. Secondly, typhoid recurrences or relapses may be distinguished by this reaction from intercurrent lung affections and other febrile complications. With a recurrence or a relapse the reaction will return or be increased; otherwise this is not the case.

The reaction is found quite frequently in phthisis, especially in severe and progressive cases. Here it suggests a bad prognosis, and is, as it were, an index to the general serious condition. Unfortunately, the reaction does not seem to be of any value in differentiating acute miliary tuberculosis from typhoid, as it is often present and very intense in the former.

In puerperal infection the appearance of the reaction is coincident with the fever.

Rüttimeyer has also observed the reaction in pulmonary actinomycosis.

The diazo-reaction must be considered as a metabolic symptom of certain diseases, which, like splenic swelling and fever, is not of diagnostic value in itself, but only when considered in connection with the other symptoms. It should also be noted that a similar reaction may be obtained after the administration of opium, morphin, heroin, dionin, tannic acid, alcohol in large quantities, chrysarobin, naphthalin, phenol, cresol, creosote, and guaiacol. The fact must consequently be borne in mind before drawing conclusions as to the diagnostic value of the diazo-reaction.

The so-called *egg-yolk reaction,* as described by Ehrlich, is said to be somewhat characteristic of pneumonia just before and during the crisis. It is a preliminary reaction, *i. e.*, a diazo-reaction which occurs before the addition of ammonia. The urine becomes deep yellow after the addition of the reagent, the color showing most distinctly in the foam. It does not turn red when ammonia is added, but becomes lighter yellow. Oppenheim found it constantly in 28 of his cases at the crisis. In some conditions we might predict the crisis from this reaction. Ehrlich attributes it to urobilinogen, a transition product of the bilirubin arising from the hemoglobin of the hemorrhagic exudate, and this assumption has been confirmed by the investigations of Thomas. (See p. 585.) The egg-yolk reaction is less sensitive than the paradimethylamidobenzaldehyd reaction for urinobilinogen described on p. 585.

EXAMINATION OF THE URINE FOR SUBSTANCES INTRODUCED INTO THE BODY FROM WITHOUT (DRUGS AND POISONS)

DETECTION OF LEAD

A shining strip of magnesium free from lead is placed in the urine and left there for some time; the deposit is dissolved in nitric acid and then tested according to the rules of inorganic chemistry.[1] If the urine contain but a small amount of lead, this method will not give the desired result; a larger quantity of the urine must be used, the organic substances destroyed with hydrochloric acid and potassium chlorate, by the method of Fresenius and v. Babo, and the lead sought for in the evaporated residue.[2] For this purpose a large amount of urine is evaporated to about one-tenth of its volume. An equal volume of 20 per cent. hydrochloric acid is added, and 3 gm. of potassium chlorate. The mixture is heated on the water-bath at 60° C. As soon as the evolution of chlorin has ceased, another portion of 3 gm. of potassium chlorate is added, and the operation repeated until the fluid no longer gives off fumes of chlorin on the further addition of the chlorate. If the liquid becomes too concentrated, more water is added. The fluid is allowed to cool, and filtered after dilution with water. The filtrate is examined for lead with hydrogen sulphid, sulphuric acid, and potassium bichromate.

DETECTION OF MERCURY

To 500 to 1000 cc. of urine are added 2 to 4 cc. of hydrochloric acid (Fürbringer). It is then digested at 60° to 80° C. for five to ten minutes in a flask with $\frac{1}{4}$ to $\frac{1}{2}$ gm. of brass-wool, and frequently shaken. The metal is washed first with water, then with alcohol, and finally with ether, and dropped into a glass tube of high melting-point, which has been prolonged into a capillary tube at the upper end. It is there brought to a red heat, the capillary end being kept uppermost. The mercury, which has become amalgamated with the brass-wool, becomes volatile and will be de-

[1] Salkowski, Practicum der physiol. u. path. f. Chemie, 1900, second edition.

[2] For the accurate procedure, see Lehmann, Zeit. f. physiol. Chem., 1882; vol. vi, p. 4, and Späth, Chem. u. mikroskop. Untersuchungen des Harnes, 1903, p. 393.

posited as a mirror at the capillary end of the tube. If a particle of iodin is evaporated in the tube, the deposit will be colored red by the formation of mercuric iodid. (In reference to other methods, see Späth, l. c., p. 399 et seq.)

DETECTION OF IODIN

Iodin occurs in the urine as potassium iodid after the internal and external administration of iodin or one of its preparations. It may be easily demonstrated as follows: A few cubic centimeters of urine are boiled with a piece of starch about the size of a pea until the latter is dissolved. After cooling, 1 cc. of a 1 per cent. sodium nitrite solution is added, the fluid is carefully stratified over concentrated sulphuric acid. If iodin be present, a blue-violet ring that gradually disappears is formed at the line of junction of the two fluids. In this test iodin is liberated from the potassium iodid by the nitric acid, and unites with the starch to form blue iodid of starch.

Another way is to add to the urine 1 cc. of dilute sulphuric acid (1: 1) and 0.5 cc. 1 per cent. sodium nitrite solution[1] and ½ cc. of chloroform, and then shake gently. If iodin be present, the chloroform which settles to the bottom will be colored a rose red to violet, due to the solution in the chloroform of the free iodin.

To prove that a patient has really taken a drug prescribed, introduce a grain or two of potassium iodid into the prescription. Iodid should then be demonstrated both in the urine and in the saliva. The detection of iodin is used in the desmoid and glutoid tests. (See pp. 433 and 506.)

Both the above tests are very delicate. But if the urine contain but a very slight trace of iodin, the chloroform test may not be specific, since the nitric acid may set free indol and skatol pigments as well as urorosein (see p. 582), and so tinge the chloroform reddish. But in this case the urine itself usually appears more deeply colored than the chloroform. The starch reaction may not be of much help in deciding in such a case, because the blue ring of the iodid of starch may be simulated by an indican reaction, for in a urine so rich in such chromogen not only calcium hypochlorite, but sometimes even nitric acid (see p. 577), will produce the change. Here, however, it is easy enough to show that the nitric acid alone is capable of producing this blue ring without the addition of any starch.

Palladium chlorid furnishes still another iodin reaction. The urine suspected to contain iodin is strongly acidulated with hydrochloric acid, and then a few drops of a moderately saturated solution of palladium chlorid in hydrochloric acid[2] are added. If iodin be present, a brown discoloration occurs, and gradually a black precipitate. This reaction has but one meaning, but it is much less delicate than the starch or the chloroform reaction.

DETECTION OF BROMIN

The test for bromin is performed in exactly the same way as the iodin test with chloroform, except that a few drops of a calcium hypochlorite solution and hydrochloric acid are used to liberate the bromin. If bromin be present, the chloroform will be colored yellowish brown by the free bromin. This test, although much less delicate than the iodin test, is sufficiently accurate to recognize the therapeutic ingestion of large doses of bromin salts. To add to the uncertainty of this test, we must remember that the chloroform can also be tinged yellow by some of the urinary coloring-matters. To prevent this latter source of error, 10 cc. of the urine, to which have been added 2 cc. of caustic potash and 2 cc. of potassium nitrate, are incinerated, the ash dissolved in water, and the resulting solution tested for bromin, as above.

A. Jolles[3] has described an admirable test which is quite simple. It depends upon the fact that bromin can be freed from the urine by potassium permanganate in acid solution, and that such free bromin gives a red color with *p*-dimethylphenylendiamin. Filter-paper is moistened with an aqueous solution of the hydrochlorid of *p*-dimethylphenylendiamin, dried, and cut into strips. Ten cc. of urine are acidulated in a narrow-necked flask with H_2SO_4, saturated with potassium permanganate. The color is now a permanent red. A moist strip of the above test-

[1] The author previously suggested commercial nitric acid, but as the reagent not infrequently contains iodin, the above reagent is better.

[2] This solution is prepared by adding 1 gm. of palladium chlorid to a few drops of hydrochloric acid, allowing it to stand for a day, and then diluting the resulting solution with enough hydrochloric acid to make a faintly transparent brown solution.

[3] Wien. klin. Rundschau, 1898, No. 12.

paper is suspended in the neck of the flask, and the latter is warmed over a water-bath. If bromin be present, the paper will be colored from violet, through blue and green, to a brown. Iodin and chlorin present other brownish shades different enough not to be confusing.

The demonstration of bromin in the urine is of no special interest, except, of course, in verifying a diagnosis of suspected bromism.

DETECTION OF SALICYLIC ACID AND SALOL

Ferric chlorid is added, drop by drop, to the urine. In the presence of these compounds the solution becomes more or less violet. The test is delicate and can be used for control after the administration of these substances. The salicylic acid is partly eliminated as salicyluric acid, which gives the same reaction. To distinguish between salicylic acid and aceto-acetic acid see p. 602. For the detection of salicylic acid in urine containing bile-pigments, see p. 577.

DETECTION OF PHENOL

Phenol appears in the urine largely as phenol sulphuric acid. Ferric chlorid will produce a violet-blue color in the distillate from a phenol urine to which 5 per cent. sulphuric acid has been added. With saturated bromin water, a precipitate of tribromphenol is produced. Millon's reagent gives a red color on heating. The last reaction is given by a number of other substances. According to Salkowski, the following short method may be used to detect phenol. A control test must be made with normal urine. The urine is heated to boiling in a test-tube with nitric acid. The urine gives off an odor resembling oil of bitter almonds due to the formation of orthonitrophenol. When the urine is perfectly cold, bromin water is added. A precipitate will be formed of tribromphenol. Normal urine treated in this way will remain clear or give a very faint opalescence. A second portion which has been boiled with nitric acid is made alkaline with sodium hydroxid. With urine containing phenol an orange-red color is produced to orthonitrophenol sodium. Phenol urine turns dark to black upon exposure to the air. This is due to the fact that it contains hydroquinone and pyrocatechin, which form dark-colored derivatives upon oxidation.

DETECTION OF ANTIPYRIN

The urine appears dark and is dichroic, in reflected light greenish, in transmitted light reddish. A brownish-red color gradually appears upon the addition of ferric chlorid solution.

DETECTION OF THALLIN

The urine is yellowish-green to dark brown, and turns brownish-red upon the addition of ferric chlorid solution. If the urine be shaken with ether, the latter will be tinged green[1] upon the addition of ferric chlorid.

DETECTION OF PHENACETIN

The urine is dark yellow, and turns reddish-brown upon the addition of ferric chlorid solution. The color gradually becomes black after prolonged standing.

DETECTION OF ANTIFEBRIN

The urine is extracted with chloroform, and to the extract mercuric nitrate is added. The mixture is then heated, and if a green color is produced,[2] antifebrin is present.

DETECTION OF PYRAMIDON

The urine is frequently clear, purplish-red in color, and deposits a sediment consisting of small red needles. If the urine be mixed with an equal volume of a 2 per cent. solution of ferric chlorid, a dark-brownish amethyst color is produced. According to Jolles, a violet ring, gradually becoming red, is obtained when the urine is carefully covered by a layer of dilute alcoholic solution of iodin (a 10 per cent. tincture of iodin diluted with 10 parts of alcohol).

[1] v. Jaksch, Zeit. f. klin. Med., vol. viii, p. 551.
[2] Yvon, Jour. de Pharm. et de Chemie, 1887, No. 1.

DETECTION OF TANNIN

Tannin is eliminated in the urine partly as gallic acid. Urine which contains tannic and gallic acids will turn blue-black upon the addition of ferric chlorid solution (ink reaction).

DETECTION OF BALSAM OF COPAIBA AND SANDALWOOD OIL

After the administration of balsam of copaiba the urine will reduce cupric oxid (Trommer's test), but not bismuth (Nylander's test). If hydrochloric acid is added to the urine drop by drop, a precipitate of resinous acids appears, with a reddish to violet coloration. Also after the use of sandalwood oil the urine possesses reducing properties, and will exhibit a precipitate of resinous acids when hydrochloric is added, but with a reddish-brown color. Karo claims that this color is not characteristic. Alexander[1] emphasizes the fact that the intensity of the resinous acid precipitate is not proportioned to the color reaction produced, and that, with regard to the amount of the resinous acid excreted, individuals differ greatly when the same dose of copaiba balsam or sandalwood oil has been administered.

DETECTION OF SANTONIN

Santonin urine is of a saffron-yellow to greenish color. The addition of sodium hydroxid will turn it a rose-red shade. If this rose pigment is shaken with amyl alcohol, it will be immediately dissolved by the latter, giving it a beautiful and intense coloring, while the urine will become decolorized.

DETECTION OF EMODIN, CHRYSOPHANIC ACID, AND SUBSTANCES RELATED THROUGH THE OXYMETHYLANTHRAQUINONE GROUP, RHUBARB, SENNA, RHAMNUS (CASCARA SAGRADA), ALOES

After the ingestion of rhubarb, of the different kinds of rhamnus (R. frangula and R. purshiana or cascara sagrada), of senna, and of large doses of aloes, the urine will be tinged a brownish-yellow, and upon the addition of an alkali (sodium, potassium, or ammonium hydroxid) will become more or less distinctly red. This peculiarity depends upon the presence of emodin (trioxymethylanthraquinone) and of chrysophanic acid (dioxymethylanthraquinone). These substances are excreted in the urine partly as such and partly in combination. Even after the external use of chrysarobin the urine sometimes exhibits the same peculiarities, probably because chrysophanic acid is formed in the body from chrysarobin. Urine containing one of these substances differs from santonin urine in this respect: the red coloring-matter produced by the addition of alkalis will not dissolve in the amyl alcohol. The reaction common to chrysophanic acid and emodin, and recently named the *oxymethylanthraquinone reaction*, has been modified and made more delicate, according to Tschirch, by boiling the urine in a test-tube with 1 or 2 drops of caustic potash, in order to split up the combined bodies, then acidulating with HCl, extracting with ether, and shaking the ether with ammonia. After a short delay the ether separates from the ammonia, and the latter is tinged a beautiful cherry-red. Chrysophanic acid passes from the ether into the ammonia with difficulty, so that, if the ether remains yellow despite the red coloration of the ammonia, we are justified in deciding upon the presence of chrysophanic acid instead of emodin.

QUANTITATIVE URINARY ANALYSIS

Preliminary Note.—Since in the quantitative analysis of any urine the amount of the particular constituent excreted in twenty-four hours is required, the specimen examined must be a portion of a well-mixed twenty-four-hour urine.

QUANTITATIVE ESTIMATION OF UROCHROME

Klemperer[2] has made a noteworthy attempt to attach a diagnostic value to the amount of normal urinary pigment contained in the urine. The normal urinary

[1] Deut. med. Woch., 1893, No. 14, p. 324.
[2] Berlin. klin. Woch., 1903, No. 14, p. 314.

pigment, and frequently the only one, is urochrome; it holds a close chemic relation to urobilin, into which it may be converted by cautious oxidation. According to Klemperer, the normal color of the urine corresponds approximately to 0.15 per cent. urochrome solution. He determines the amount of contained urochrome colorimetrically by comparison with a solution of "Echtgelb" (Leitz). Klemperer prepares this solution for comparison by dissolving 0.1 gm. of dry "Echtgelb" in a liter of water, and diluting 5 cc. of this solution to 90 cc. According to Klemperer, the shade of this solution of "Echtgelb" (1: 180,000) corresponds to 0.1 solution of urochrome, and by diluting the urine or the test solution, the quantity of contained urochrome may easily be determined by the colorimetric method. The urine and the test solution must, of course, be contained in vessels of the same shape when the comparison is made. Stronger solutions of "Echtgelb" cannot be employed, since their color does not agree with that of urine. Should the urine contain considerable quantities of other pigments, such as urobilin or hematoporphyrin, an exact colorimetric estimation of the urochrome is, of course, impossible. Klemperer, nevertheless, believes that if the presence of these other pigments is not disclosed by absorption-bands in the spectroscopic examination (urochrome absorbs light diffusely), the method given above will be sufficiently accurate. He also believes that the estimation of the daily excretion of urochrome furnishes an indication of the functional activity of the kidneys, since he assumes that urochrome is formed in the kidneys. It is, nevertheless, clear that if the latter assumption be incorrect, and it has not yet been proved, the amount of excreted urochrome is not of such simple significance, since it would not depend upon the kidneys alone, but also upon the unknown function upon which the formation of urochrome in the body is dependent. The fact that pale urine is frequently excreted in uremia could also be due to the fact that, in addition to the impairment of the excretory function of the kidneys, other important functions holding some relation to the formation of urochrome are also implicated.

QUANTITATIVE ESTIMATION OF PROTEINS. ESTIMATION OF TOTAL ALBUMIN (SERUM-ALBUMIN + SERUM-GLOBULIN)

ESTIMATION BY OBTAINING AND WEIGHING PURE (COAGULABLE) PROTEIN, OR BY KJELDAHL'S METHOD

An exact quantitative estimation of coagulable protein must depend upon a complete precipitation of the protein by boiling after the addition of dilute acetic acid (2 per cent.) and the addition of $\frac{1}{10}$ volume of saturated sodium chlorid solution, which facilitates the coagulation of the protein. (See Removal of Protein from Urine, p. 566.) The precipitate must then be washed, and dried upon a dry, weighed filter at 110° to 120° C. to a constant weight, the dried residue weighed, and the weight of the dry filter subtracted. To save time in drying the precipitate, the amount of urine should be small, so that the weight of the dry protein will not exceed 0.2 to 0.3 gm. (preliminary estimation). (See below, Estimation of Quantity of Protein According to Esbach.)

Proteins are exceedingly hygroscopic; hence, the weighing should be very carefully carried out. The material should be placed between watch-glasses, with the ground edges carefully applied to each other. For very great accuracy the albumin precipitate must be first washed with alcohol and ether, in order to remove the fat before drying, and finally the content of ash determined and subtracted. With urines containing a large amount of albumin, Salkowski recommends precipitating a measured volume of the urine with 10 to 20 volumes of 95 per cent. alcohol, heating the mixture on the water-bath. The precipitate is collected on a filter and washed with hot water. The procedure is then the same as above. The amount of protein in the precipitate may be estimated by hydrolyzing the precipitate by Kjeldahl's method, and multiplying the amount of nitrogen found by 6.3. This gives the amount of protein.

REFRACTOMETRIC ESTIMATION OF ALBUMIN

Following the work of Ellinger[1] in 1891 and Riegler in 1895[2] on the estimation of albumin by means of the refractive index, recently, owing to the construction of a convenient Pulfrich refractometer, this method has again been suggested. It is, however, in its present form not entirely free from error, and the author merely refers to the more recent investigations on the subject.

Strubell, Cong. f. inn. Med., 1900, and the same author, Arch. f. klin. Med., 1901, vol. lxix; S. Strauss and B. Chajes, Zeit. f. klin. Med., 1904, vol. lii; Reiss, Arch. f. exp. Path. u. Pharm., 1904, vol. li.

ESTIMATION OF ALBUMIN BY TITRATION ACCORDING TO DENIGÉS

The following solutions are used:

1. Potassium mercuric iodid (13.55 gm. of mercuric chlorid are brought into a liter flask with 80 to 100 cc. of cold distilled water and 36 gm. of potassium iodid added). Solution is obtained by shaking and the whole made up to 1000 cc.
2. Decinormal silver nitrate solution.
3. Ammoniacal potassium cyanid solution, which is equivalent to vigintinormal silver solution. This is made by mixing equal volumes of ammonia and a decinormal potassium cyanid solution. The latter is prepared by dissolving in a flask holding more than 1000 cc. 16 to 18 gm. of the purest potassium cyanid in 500 cc. of water. To this 550 to 600 cc. of water and 10 cc. of sodium hydroxid (S. G. 36 Beaumé) are added. In order to standardize the solution, 10 cc. are taken, diluted with 100 cc. of water, 10 cc. of ammonia, and 1 cc. of 10 per cent. potassium iodid. The mixture is titrated with decinormal silver solution until a permanent precipitate takes place. If x cc. have been used and this is greater than 10, the difference shows the excess in strength over the silver solution, and to each 10 cc. of the cyanid the difference must be added to bring the cyanid equivalent to the silver. In winter the solution must be controlled once a month, in summer every fortnight, as it changes its strength. A correction must then be made for this change.

Principle.—When potassium mercuric iodid is added to a solution containing albumin, the latter is precipitated, and combines with a certain amount of the mercury. If the precipitate be filtered off and the loss of mercury ascertained, an estimate of the amount of albumin may be made. If one adds to a potassium mercuric iodid solution of the above composition a measured amount of the cyanid, potassium mercuric cyanid, potassium iodid, and potassium cyanid are obtained. If decinormal silver solution be added, a permanent precipitate of silver iodid will occur when all the potassium cyanid is changed to silver cyanid. If before the addition of the potassium cyanid a part of the mercury has been combined with albumin, there will be more potassium cyanid uncombined, and hence, a greater amount of silver solution will be necessary to combine with the cyanid. Hence, the amount of mercury combined with the albumin, and consequently the albumin itself, may be estimated.

Process.—The approximate amount of albumin is found either by Denigés' method, Roberts-Stolnikow's method, or the Esbach tube.

If the urine contains less than 0.1 per cent. of albumin, 20 cc. of the potassium mercuric iodid solution, 2 cc. of acetic acid, and 150 cc. of urine are placed in a flask and the mixture made up to 200 cc. The precipitate is filtered off, and 25 cc. of the ammoniacal potassium cyanid added to 125 cc. of the filtered urine. The mixture is shaken for two to three minutes, and again filtered. One hundred and twenty cc. of this second filtrate are then titrated with decinormal silver nitrate to a permanent precipitate. The number of tenths of a cubic centimeter used, less 48, which is the number of tenths which are necessary to combine with 10 cc. of potassium mercuric iodid, and 20 cc. of potassium cyanid, corresponding to 120 gm. of the second filtrate, gives the number of decigrams of albumin per liter. If, for example, the number of tenths = 57, the amount of albumin in 1 liter is 57 − 48 = 0.9. The constant 48 must be controlled from time to time by titrating 10 cc. of the potassium mercuric iodid solution, 20 cc. of the ammoniacal potassium cyanid, and 100 cc. of water. The titration must give 4.8 cc. If other values are found, for example, 4–7, 4.5, the value to be subtracted must be 47 or 45 as the case may be.

In the second case, where the urine contains more than 0.11 per cent., the urine is so diluted that the amount in the diluted urine falls under this limit. This method

[1] Jour. f. prakt. Chem., 1891, (2) zliv, 256.

[2] Wien. med. Blätter, 1895, 48, Maly's Jahresberichte, 1895, 261. Referred to in Neubauer and Vogel, Harnanalyse, 1898.

gives practically identical values with those obtained by weighing the albumin. If the urine contains less than 0.002 per cent., the method is uncertain, and one uses the diaphanometric method of the same author.

DIAPHANOMETRIC METHOD OF DENIGÉS

A standard albumin solution is prepared, by obtaining a urine containing at least 0.2 to 0.4 per cent. of albumin. The amount contained is exactly estimated by weighing. The urine is so diluted that it contains exactly 0.1 per cent. of albumin. Sodium fluorid and thymol are then added to preserve it.

In 5 test-tubes of the same size, which are marked at 10 cc., and which are labeled 1, 2, 4, 8, 12, are placed 0.1, 0.2, 0.4, 0.8, 1.2 cc. of the standard solution, and the tubes filled to the mark with water or urine free from albumin. In a similar tube to the standard tube one places 10 cc. of the urine to be examined. To all the tubes one adds 2 cc. of a 5 per cent. solution of sodium metaphosphate and 5 drops of sulphuric acid. The tubes are agitated and placed in a water-bath, and heated to boiling for five minutes. After taking from the water-bath they are wiped dry and a comparison of the tube containing the urine to be examined made with the standard tubes. The intermediate amounts may be estimated. If the urine contains more than 0.012 per cent. of albumin, it must be diluted for comparison.

ESBACH'S ESTIMATION OF PROTEIN

This method consists in determining the *volume* of protein which is precipitated from a definite amount of urine by a certain solution. A graduated test-tube of thick glass, called an albuminimeter (Fig. 242), is filled to the mark U with the acidified urine to be examined, and then a solution (10 gm. of picric acid and 20 gm. of citric acid in 1 liter of distilled water) for precipitating the proteid is added up to the mark R. The tube is closed with a rubber cork, and the liquids mixed by repeated inversion without shaking. The glass is now set upright in a test-tube rack. The precipitated protein gradually settles to the bottom, and after twenty-four hours the height of the layer can be quickly seen. The graduations indicate the grams of protein in the liter. With some instruments the graduation reads as high as 1.2 per cent. If the amount of protein is so large (0.5 per cent.) that the precipitate settles unevenly, it is safer to dilute the urine once or twice, or even four times, before performing the test. In Esbach's method the limit of accuracy for a moderate amount of protein is perhaps 0.1 per cent. If the amount of protein is large, or if it is less than 0.05 per cent., the chances for error become considerable. A very small quantity will not sediment, so that it cannot be estimated by this method. The empirical graduation of Esbach's albuminimeter presupposes, of course, the average room temperature. The result will be decidedly different if the surrounding temperature varies much from the normal. If the urine contain much potassium, potassium kreatinin picrate may be precipitated (Pribram). If the urine contain a considerable quantity of resinous acids—*e. g.*, after ingestion of the balsams or of sandalwood oil—this method cannot be employed, because these acids will be precipitated by the picric acid along with the protein.

Fig. 242.—Esbach's albuminimeter.

ROBERTS-STOLNIKOW'S (BRANDBERG'S) METHOD FOR THE ESTIMATION OF PROTEIN

A method described by Roberts and Stolnikow simultaneously, and then tested more accurately by Brandberg, can be recommended if we do not happen to have an albuminimeter. This test depends upon the fact that the turbidity of protein in the nitric acid test appears more or less quickly according to the amount of protein contained in the urine. If the urine contains 0.0033 per cent. of protein, the cloudiness first appears within two and one-half to three minutes. By diluting the urine sufficiently to cause the turbidity to appear within that interval, the amount of protein actually contained in the specimen can be readily determined. Naturally, great care must be exercised in performing the reaction. If a cloudiness occurs inside of three minutes, we employ a dilution of 1:10 (A). If this dilution is still not sufficient, mixture B may be prepared by diluting 1 part of A with 2 parts of water. If even this mixture (B) is too concentrated, we make up a third dilution (C), consisting of 1 part of B with 4 parts of water; and again, if necessary, a fourth dilution (D), consisting of 1 part of C with 1 part of water.

A	corresponds to	0.033	per cent.	of protein
B	"	0.10	"	"
C	"	0.50	"	"
D	"	1.00	"	"

If the right mixture has not been found, other intermediary ones may be made.

If the urine contains either nucleo-albumin or resinous acids, this method, like that of Esbach, is not available, because nitric acid precipitates both of these bodies along with the protein (p. 565).

APPROXIMATE ESTIMATION OF THE AMOUNT OF ALBUMIN IN THE URINE ACCORDING TO DENIGÉS WITH TANRET'S REAGENT

As a preliminary to the titration of albumin in the urine, Denigés makes a test with Tanret's reagent. The solution is prepared by dissolving 13.55 gm. of mercuric chlorid, 36 cc. of potassium iodid, and 100 cc. of water. Two hundred cc. of acetic acid are added, and the whole diluted to 1000 cc. Urines when treated with one-tenth their volume of Tanret's reagent and boiled give a flocculent precipitate in case they contain more than 0.12 to 0.15 per cent. of albumin. With small concentrations an opalescence occurs. The dilution requisite to produce an opalescence is ascertained, and from this a calculation is made of the approximate amount of albumin in the urine. If, for example, 5 cc. of urine must be diluted with 100 cc. in order to reach this point, the urine contains approximately $0.15 \times 20 = 3$ gm. of albumin per liter or 0.3 per cent.

QUANTITATIVE ESTIMATION OF THE TOTAL GLOBULIN, EUGLOBULIN, AND PSEUDOGLOBULIN, AND THE RELATION TO SERUM-ALBUMIN (F. A. HOFFMANN'S PROTEIN QUOTIENT)

Quantitative Estimation of the Total Globulin

The urine is treated as for the detection of globulin, described on p. 567. The globulin precipitate is coagulated by heat and weighed. According to Emerson, this is done as follows: The urine is made alkaline with ammonia to precipitate the phosphates, filtered, and to the filtrate an equal volume of a saturated solution of ammonium sulphate added. The mixture is allowed to stand several hours, and then poured through a dry filter. The precipitate is washed with half-saturated ammonium sulphate until it is free from chlorin. The funnel and filter are heated in an air-bath to 110° C. for thirty minutes. The globulin is rendered insoluble. It is then washed with hot water until it is free from sulphates, and finally with alcohol. It is dried to constant weight at 110° C. The amount of urine should be such that the weight of the precipitate is not over 0.3 gm.

Separate Estimation of Euglobulin, Pseudoglobulin, and Serum-albumin

This is done, according to Zack and Necker,[1] in the following way, which is based on the fact that euglobulin is precipitated by one-third saturation, and pseudoglobu-

[1] Deut. Arch. f. klin. Med., 1907, lxxxviii, 545.

lin by one-half saturation with ammonium sulphate. A portion of the twenty-four-hour amount of urine is neutralized with ammonia or with sulphuric acid and filtered. Fifty cc. of the filtrate are measured off, and to this filtrate 25 cc. of a saturated solution of ammonium sulphate (specific gravity, 1.252) added. The precipitate is allowed to stand over night. The precipitate is then filtered off and washed with one-third saturated ammonium sulphate until the washings do not show the slightest trace of coagulation with heat. Both filtrate and wash-water are collected, and by adding one-third of the total volume of saturated ammonium sulphate, half saturation is secured, and the pseudoglobulin precipitated. This is allowed to stand and filtered off. This is washed with one-half saturated ammonium sulphate. If one wishes to estimate the remaining albumin, the filtrate is made acid with acetic acid and coagulated by heating. This is filtered, washed, and weighed. The first two precipitates are digested with water for a long time, to bring them into solution; acetic acid is added, and coagulation effected by heating. The process used is that of Emerson.

In amyloid kidney and in orthostatic albuminuria the globulins appear to be the principal constituents of protein present in the urine. According to Oswald, euglobinuria is the mildest form of albuminuria, and it is also often found in the larger quantity in febrile conditions. In the acute stages of parenchymatous nephritis much euglobulin is excreted.

F. A. Hoffmann[1] describes an albumin-protein quotient which is formed from the relation of serum-albumin to globulin. In acute nephritis this has a certain amount of diagnostic value, because with the relief of the patient the quotient rises. The prognosis is better the higher the quotient. This, however, only holds for acute nephritis. Similar results have been obtained by Lecorché and Talamon.

QUANTITATIVE ESTIMATION OF GLUCOSE

In diabetes mellitus the amount of sugar in the urine generally ranges from 4 to 5 per cent., but it may be as high as 10 per cent., so that in the course of twenty-four hours 1 kg. or more may be excreted.

REGARDING THE NECESSITY OF THE CLINICIAN MAKING QUANTITATIVE ESTIMATIONS OF GLUCOSE

The author cannot lose the present opportunity of pointing out to the clinician the importance of carrying out the determinations of glucose in his own laboratory. This may be done with great ease, owing to the convenient methods which are now available for this purpose. The incorrect reports, even of qualitative tests, which are sent out by druggists, commercial laboratories, and similar institutions, have often had, as the author has convinced himself, the most harmful results. The examinations are frequently made by assistants who are untrustworthy, and consequently the reports are not to be relied upon. Furthermore, no information is given as to the methods which have been employed. In allowing this very important part of a diagnosis to be done by another, the clinician lays himself open to very great mistakes, and the procedure might be easily compared to a physician turning over the auscultation and percussion of a patient to a percussor or auscultator, and giving a diagnosis from the report. The author believes that in those cases where reports are handed in of "traces of sugar" or doubtful reductions, the clinician himself is the only one who is in a position to perform the necessary control tests for pentoses, glycuronic acids, etc. In any event, the mere statement of a report of "traces of sugar" does not give any guarantee that these latter substances have been taken into consideration. There are concerns where the estimations are carried out with all care, but the physician must first assure himself of this—a precaution which is too often neglected. The author has recently seen a case where a trusting physician treated a patient for months for diabetes with the strictest diet, and thus reduced him almost to a skeleton, and it was subsequently ascertained that the report which had been given to the physician was in every respect erroneous. If the physician wishes to do the very best for his patient, he should carry out the quantitative determinations for glucose himself. Apart from the gain in the trustworthiness of the observations, it should be pointed out that in order to obtain the best results, a daily estimation, or, at least, a frequent quantitative examination of the urine of the patient should be made, in order that one may follow instantly any change in the

[1] Virchow's Arch., vol. lxxxix.

diet and so formulate a plan for treatment. Only the wealthier patients can afford to have these examinations made in properly conducted laboratories. The physician must, therefore, perform the examinations himself, just as he percusses and auscultates. If it be not done, harm results.[1] The author's attitude may be objected to on the score that the estimations require special training. But it is directly for this purpose that chemistry is required as part of a medical course. If the objection were correct, it would be a very severe criticism of modern methods of medical teaching.

ESTIMATION OF THE AMOUNT OF SUGAR FROM THE SPECIFIC GRAVITY AND THE QUANTITY OF URINE

Naunyn constructed an approximately accurate table for estimating the amount of sugar in diabetic urine, as follows:

With a daily quantity of:

2 liters	and with a	specific	gravity	between 1028 to 1030,	about	2 to 3	per cent.
3 "	"	"	"	1028 to 1032,	"	3 to 5	"
5 "	"	"	"	1030 to 1035,	"	5 to 7	"
6 to 10 liters	"	"	"	1030 to 1042,	"	6 to 20	"

The percentage of sugar in the urine can be approximately determined from the quantity and specific gravity if we deduct as much from the specific gravity found as would represent the specific gravity of a normal non-sugar urine, diluted up to the same quantity by the excessive ingestion of water. For instance, if 2 liters represent the amount of the twenty-four-hour secretion, the specific gravity would ordinarily be about 1005. Then, if the volume is still further increased by abundant water-drinking, a urine whose twenty-four-hour quantity amounts to 3 liters will have approximately a specific gravity of—

$$\frac{2 \times 1015 + 1000}{3} = 1010,$$

and one of 6 liters, a specific gravity of—

$$\frac{2 \times 1015 + 4000}{6} = 1005.$$

Now suppose a diabetic urine (*a*), whose twenty-four-hour amount equals 3 liters, and another (*b*), whose twenty-four-hour amount equals 6 liters, have the same specific gravity, 1030. The sugar contained, then, in urine *a* is sufficient alone to produce a specific gravity of $1030 - 1010 = 1020$, and in urine *b* to $1030 - 1005 = 1025$. From this the amount of sugar present can be approximately calculated by multiplying the last two figures of the specific gravity by 0.23. (See p. 623, *f*, Quantitative Areometric Fermentation Test.) This gives for urine *a*, 4.6 per cent., and for urine *b*, 5.7 per cent. Such an estimate is, of course, inaccurate, if for no other reason than that diabetes mellitus also alters the amount of urea and salts eliminated, which in turn also influences the specific gravity of the urine.

[1] The patient may be instructed to carry out the estimations for himself with the areometric fermentation method. This method excludes the greater errors, and is to be preferred to reports from a laboratory of whose trustworthiness one has not been convinced. Intelligent patients may be instructed to perform Pavy's titration for sugar. In both cases, the results should be controlled from time to time by the physician himself.

ESTIMATION OF THE QUANTITY OF GLUCOSE BY TITRATION

Fehling-Soxhlet's Method

Glucose will reduce cupric oxid in an alkaline solution to cuprous oxid. This property is the one most frequently employed in titrating for sugar, because when certain conditions are maintained, the reduction of the alkaline cupric oxid solution by the sugar takes place quantitatively. *Fehling's solution* is the one generally employed. It is prepared as follows: 34.64 gm. pure crystalline copper sulphate, 173 gm. Rochelle salt (sodium potassium tartrate), 100 cc. sodium hydroxid solution of specific gravity 1.34, distilled water up to 1000 cc.

Fehling's solution cannot be preserved in its original form. It is, therefore, advisable to keep two separate solutions, which should not be mixed until just before using. Solution 1 contains 34.64 gm. of copper sulphate dissolved in 500 cc. of distilled water, acidulated with a drop of concentrated sulphuric acid. Solution 2 contains 173 gm. of Rochelle salt with 100 cc. of NaOH solution (specific gravity 1.34), and the volume made up to 500 cc. with water. By mixing equal volumes of these solutions, a fresh Fehling's solution can be obtained for every test. This mixture contains sufficient cupric oxid, so that 10 cc. of the solution, when diluted five times with water, will be reduced to the red cuprous oxid when boiled with 0.05 gm. of grape-sugar (or, according to Soxhlet, 0.0473 gm.). If the urine contains more than 1 per cent. of glucose, it should be diluted with water, before titration, until it does not contain more than that amount. The above-mentioned rules for approximately estimating the amount of sugar from the specific gravity can be used as the basis for this procedure. As a rule, more than 5 cc. of urine are required to reduce the 10 cc. of Fehling's solution. Albuminous urine must be freed from protein by boiling the acidified urine and filtering before titration. (See p. 566.)

Method: 5 cc. of solution 1 and 5 cc. of solution 2 are mixed in a small flask, diluted with water up to 50 cc., heated to boiling, and the urine, appropriately diluted, added a few drops at a time from the buret. The mixture is kept boiling gently until it is approximately decolorized, and an abundant precipitate of the red cuprous oxid has appeared. We cannot, of course, expect to obtain accurate results with this method (Fehling's original method), because the end-reaction cannot be recognized accurately, and because a portion of the suboxid always dissolves in the ammonia liberated from the urine and becomes reoxidized. This test really gives only approximate values.

For accuracy, Soxhlet's modification should be resorted to. He pours the approximate amount of urine into the boiling Fehling's solution at once (he also uses 10 cc. of Fehling's solution diluted to 50 cc. with water), then allows the solution to boil for two minutes, and then takes the flame away. The shining meniscus at the upper margin of the fluid is his index of the end-reaction. If this persists in being still slightly blue, he repeats the test with a fresh and slightly larger volume of urine and fresh Fehling's solution until he determines the exact amount that is required to decolorize the fluid, as shown by the meniscus.

The calculation of the result is very simple. If 9 cc. of urine diluted ten times are required to reduce 10 cc. of Fehling's solution, then 0.9 cc. of urine contains 0.05 gm. of glucose.

$$0.9 : 0.05 = 100 : X$$

$$X = \frac{5}{0.9} = 5.5 \text{ gm. of grape-sugar}$$

—*i. e.*, the urine contains 5.5 per cent. of glucose.

Or if we employ the exact figures of Soxhlet:

$$0.9 : 0.0473 = 100 : X$$

$$X = \frac{4.73}{0.9} = 5.26.$$

Various other modifications of Fehling's test have been suggested to overcome the difficulty of sharply determining the change of color of the solution, *i. e.*, the end-reaction.

Practically speaking, Soxhlet's method is the only safe one for the practitioner; the others require especial practice and skill, otherwise they are too uncertain. It is well to note here that many if not most of the old results from Fehling's method were probably inaccurate; hence, we should be on our guard against accepting them unreservedly. The methods depending on the number of drops of urine which will decolorize a copper solution are suggested from time to time. These methods are absolutely unreliable and should never be used.

Glucose Titration According to Drechsel-Klimer

Klimer[1] has published Drechsel's method for sugar titration since the latter's death. It seems to offer a sharp end-reaction. It is based upon the fact that in the presence of guanin the red suboxid which is formed in Trommer's test will unite with guanin to form a less readily oxidizable combination of a white color, so that in titration with Fehling's solution to which a certain amount of guanin has been added the solution may be filtered off from the precipitate and tested for copper.

This method is accurate, but only when very pure guanin is used, and that is rather expensive. The details of the method will be found in the dissertation by Klimer, Bern, 1898.

Pavy's Sugar Titration, as Modified by the Author

The difficulties with the Fehling estimation of glucose have led to a number of modifications, some of which prevent the precipitation of the cuprous oxid and thus allow a sharp end-reaction. The best known of these is Pavy's test,[2] in which ammonia is added to the solution. The change in color is from blue to a colorless solution. The principal difficulty in the reaction is that large amounts of ammonia are evolved on boiling, which, if sufficiently prolonged, will be such that not enough ammonia is retained in the solution to prevent the precipitation of the cuprous oxid. With the access of air also the colorless solution will change to blue. Many suggestions have been made by Pavy, Moritz, and others to avoid these difficulties.

Recently the author has modified the method by using the solution more concentrated than that of Pavy.[3] By using 10 cc. of the solution and 30 cc. of water, one may boil long enough without the cuprous oxid being precipitated. The mixture does not need to be boiled vigorously, a gentle simmer being sufficient. This can be done with a microburner and an asbestos board. The fluid must, however, really boil. The addition of the urine should be so regulated that the mixture never falls below the boiling-point. The titration is performed in a flask of 75 to 100 cc. content.

Solutions Used.—Although it has been assumed that Pavy's solution is perfectly stable, it appears to the author that the same objections to a single solution apply to it as to Fehling's solution, which is well known not to be permanent when made up in one solution. For this reason the author prepares the solution in two parts which have the following composition:

1.	Copper sulphate crystals	4.158
	Distilled water to	500.000
2.	Sodium potassium tartrate	20.4
	Potassium hydroxid	20.4
	Ammonia (specific gravity, 0.88)	300.0
	Water to	500.0

The solution is made by mixing 5 cc. of Nos. 1 and 2. This is equivalent to 10 cc. of the original Pavy's solution and corresponds to 0.005 gm. of glucose. It is wise to check the correctness of this solution with a solution of pure glucose of known content. This is done by weighing out a definite quantity of purest glucose and performing a titration. The glucose must be dried at 100° C. for an hour before it is weighed. As pure glucose is more difficult to obtain than cane-sugar, Pavy recommends that pure cane-sugar be inverted and the solution used for control. Cane-sugar is dried at 100° C. for an hour and 0.25 gm. weighed out. It is dissolved in 50 cc. of 2 per cent. citric acid solution and boiled for seven minutes. The cane-sugar is changed to glucose and fructose. After cooling, it is made neutral with potassium hydroxid and made up to 250 cc. In this way a 0.1 per cent. sugar solution is obtained, which corresponds exactly to a 0.1 per cent. glucose solution in its reducing activity.

The Titration.—Five cc. each of solutions 1 and 2 are placed in a flask holding 75 to 100 cc., and 30 cc. of water added. The contents are heated over an asbestos

[1] "Ist Zucker ein normaler Bestandteil des Harnes unserer Haussäugetiere," and "Zwei neue klinische Methoden der quantitativen Zuckerbestimmung im Harne," I. A. D., Bern, 1898.

[2] Physiologie der Kohlehydrate, Deuticke, 1895.

[3] Deut. med. Woch., 1905, No. 36.

board with a burner which can be regulated. The urine (if it contains albumin is freed from this substance) is diluted and placed in a buret. The flow of urine from the buret is best controlled by a screw pinch-cock.

In order to secure exact results the urine must be so diluted that the amount necessary for the complete reduction of the Pavy's solution is a fairly large amount. On the other hand, the amount must not be so large as to decrease the concentration of alkali in the solution. The urine is added drop by drop, or in small amounts at a time, taking care that the boiling is never interrupted. The amount added may be more rapid at first. Toward the end of the reaction the urine should be added more slowly, as the reaction is slower at this time. The end-reaction is usually very easily observed. The flask is best held over a sheet of white paper. For clinical purposes the author has recently modified the process, avoiding the use of a buret. For this purpose 10 cc. of the urine or the diluted urine are placed in a measuring cylinder accurately graduated, and the urine delivered into the flask with a fine pipet. The amount delivered is ascertained from what is left in the cylinder after the titration.

The Dilution of the Urine.—The best results are obtained when the amount of urine necessary for decolorization is between 5 and 10 cc. This corresponds to a sugar-content of ½ to 1 per 1000. Control estimations with the polarimeter have shown that the results are accurate. Hence, the urine should be diluted to give a titration within these limits. To do this one must make a preliminary titration in order to find the content of the undiluted urine. This preliminary titration must be carried out with great care with urines containing much glucose, in order that the end-reaction is not overstepped. With a urine containing about 5 per cent., a dilution of 1: 50 is necessary. Some of the less important details concerning the operation are given in the author's original paper.

Errors in the Method.—As it is necessary to dilute the urines of severe diabetics, one must ascertain whether this dilution has an effect on the accuracy of the method. With dilutions of 1: 50 the error in titration is multiplied by that factor and might seriously vitiate the results. The presence of other reducing substances than glucose in the urine also influences the results, but experiments made by Ryser in the author's laboratory have shown that the results do not influence the practical use of the method. Pavy's method has also been used by Kumagawa and Suto in another modification and has been found to be accurate. The form of the method which the author has given above is the only one which—(1) permits performance without any very great practice; (2) is simple and quick.

Lehmann's Iodometric Titration Method for Glucose[1]

In this method a definitely measured amount of urine is boiled with Fehling's solution [just as in Soxhlet-Allihn's (below).—Ed.] and the copper which remains in solution in the filtrate is titrated. This is accomplished by adding a measured amount of potassium iodid solution of a definite concentration to the filtrate acidified with sulphuric acid. Iodin, which is set free according to the equation $2CuSO_2 + 4KI = 2K_2SO_4 + Cu_2I_2, + I_2$, is then titrated with sodium thiosulphate, using starch paste as an indicater. Every atom of free iodin corresponds to one atom of copper in the solution. As this method is very perfectly replaced by the author's modification of Pavy's method, reference to the details of its performance is made to the original papers and to the former edition of this book.

Titration of Glucose According to Gerrard Williamson

This is a similar method to that of Fehling, but the difficulty of the end-reaction is avoided by added ferrocyanid of potassium. Burroughs Wellcome and Co. have made up tablets containing the necessary reagents. The directions for performing the test are given with the tablets.

SOXHLET-ALLIHN'S METHOD OF GLUCOSE ESTIMATION[2] AS MODIFIED BY AMBÜHL

This is a thoroughly accurate method, perhaps the most reliable of all, and certainly to be recommended for scientific investigation. It is rather too compli-

[1] Arch. f. Hygiene, vol. xxx, and Zeit. f. anal. Chemie, 1898, part 4, and Pharm. Post, 1898, No. 30. Cf. also E. Riegler, Zeit. f. anal. Chemie, 1898, part 1, and Benjamin, Deut. med. Woch., 1898, No. 35, p. 552.

[2] Jour. f. prakt. Chemie, Neue Folge, 1880, vol. xxii, p. 52.

cated for the practising physician, but in a clinical laboratory, after the necessary apparatus is once put together, it may be performed in a reasonably short time. In this method a definite excess of Fehling's solution is partly reduced by a measured volume of urine; after filtering off the solution the red cuprous oxid previously formed is collected upon an asbestos filter, reduced in a current of hydrogen, and the resulting metallic copper weighed, from which the amount of sugar contained in the urine can be calculated. Ambühl[1] has simplified this method by weighing the cuprous oxid directly without reducing it to metallic copper. As the method is less suitable for clinical purposes than the titration method described above, it is not described in detail. A full description will be found in the last edition of this work.

COLORIMETRIC ESTIMATION OF GLUCOSE

Because of the blue color peculiar to combinations of glucose in alkaline solution with copper, and the blue color of copper combinations in general, the author has made an effort to utilize this color in one way or another for the purpose of estimating colorimetrically the quantity of glucose in the urine. He has conducted numerous experiments, and will briefly report the results.

A conceivable method is to add to a constant amount of sodium hydroxid a constant amount of copper sulphate solution, which is so chosen that the copper is always in excess, *i. e.*, when, subsequently, sugar containing urine is added, the copper cannot be held entirely in solution, but is sufficient, in spite of the sugar, to cause a precipitate of cupric hydroxid. Urine, suitably diluted, if necessary, is added in measured quantities, and the precipitate filtered from the deep-blue solution by means of an asbestos filter. The intensity of the color is determined colorimetrically and the quantity of the sugar estimated in this way. The solution may be diluted and compared with a test-solution of copper kept in a hermetically sealed tube. It has, however, been proved that this method is unreliable. The intensity of the color proves to be quite independent of the amount of sugar added, giving the impression that only small quantities of sugar enter into the blue combination. For instance, we found that it was quite immaterial whether a 0.5 or a 1 per cent. solution of sugar was added to the constant quantity of sodium hydroxid and copper sulphate.

Another method of colorimetric estimation proved equally unreliable. Copper sulphate solution is added drop by drop from a buret to a solution containing equal parts of sodium hydroxid and of the urine to be examined, until the excess of copper commenced to separate as cupric hydroxid. The shade of blue is estimated colorimetrically, but, just as before, the intensity of the color appears to be quite independent of the amount of sugar. In these experiments a 0.5 and 1 per cent. sugar solutions hold in solution about an equal amount of copper oxid. For this reason one may not draw conclusions as to the quantity of sugar contained in the urine from the volume of copper sulphate solution necessary to produce cloudiness.

One might endeavor to utilize the reduction test colorimetrically. After performing the reduction (Soxhlet-Allihn, p. 621) and filtering off the suboxid the quantity of non-reduced copper in the filtrate might be estimated colorimetrically instead of iodometrically. Even this method is not practical, for we found that the color-intensity of Fehling's solution with constant quantities of alkali and Rochelle salt does not run parallel with the amount of copper contained.

However, the following method of utilizing the reduction test colorimetrically gives approximate results. The test is the same as Soxhlet-Allihn's up to the filtering off of the reduced suboxid, for iodometric estimation. The cuprous oxid or the reduced copper is not determined by weighing, but nitric acid is poured on the asbestos filter until the red oxid is dissolved. Water is next poured over the filter, and the quantity of copper contained in the solution estimated colorimetrically by comparing with a copper solution of known strength. We began by using a solution of copper nitrate, so as to have exactly comparable conditions. We found, however, that its color was exactly that of a copper sulphate solution containing an equal amount of copper, and so have since used the copper sulphate solution utilized in preparing Fehling's solution.[2] In two graduated cylinders of equal diameter are placed respectively some copper sulphate solution and an equal volume of the nitric acid solution of cuprous oxid. Water is then added to the

[1] Ambühl, Chemikerzeitung, 21, I. Sem., p. 137.

[2] This is explained by the assumption that the color is dependent only on the copper ion which is present in equal quantities, or, at least, in equal dissociation in both solutions.

darker of the two solutions until the shade of color of the two is the same. The amount of copper contained in the two solutions is then proportional to their volumes, so that it becomes possible to estimate not only the amount of copper reduced, but also the amount of sugar in the urine, inasmuch as we know just how much glucose corresponds to each cubic centimeter of the copper sulphate solution. This method of employing graduated cylinders only, and without accurate colorimetric apparatus, gives only approximate values, which are far less accurate than the results obtained by weighing the copper or cuprous oxid or by Pavy's method. The practising physician, however, who is not familiar with the technic of the more accurate methods, and who desires a method more rapid than the fermentation test, may obtain with this method fairly satisfactory approximate results. By using accurate colorimetric apparatus, the correctness of the values obtained is much greater.

QUANTITATIVE FERMENTATION TESTS FOR GLUCOSE

Upon the addition of yeast, glucose possesses the property of fermentation—*i. e.*, of splitting into alcohol and carbon dioxid. Three tests, based upon three different results of this property, have been devised to determine the quantity of sugar in urine.

Robert's Quantitative Areometric or Densimetric Test.—This is based upon the fact that fermentation considerably diminishes the high specific gravity of sugar-containing urine. From this difference in specific gravity before and after fermentation the percentage of sugar may be determined.

The technic of the test is as follows: The specific gravity of the diabetic urine is estimated in the ordinary way. A piece of compressed yeast (not containing sugar, or, if so, washed out with water) the size of a hazelnut is then added to a definite amount of urine (about 100 cc. are sufficient for testing the specific gravity readily). The mixture is shaken gently, loosely covered with a piece of paper or an inverted beaker, and allowed to remain at the room temperature for twenty-four to thirty-six hours. When fermentation is complete, the yeast will settle to the bottom, the foam will no longer form, and the fluid will become clear above. To be perfectly sure that the fermentation is completed, Trommer's test can be employed. The specific gravity of the completely fermented urine is then determined. If the yeast which has settled to the bottom is stirred up, the urine must first be filtered. If the filtrate is not absolutely bright, a small quantity of magnesia usta is added and the filtration repeated. The urine, which has been previously measured, must be brought to the original volume to make up for loss by evaporation. Determinations of the specific gravity made with the unfiltered urine do not give accurate results. If the difference between the two specific-gravity estimations (before and after fermentation) is multiplied by the empirical number 0.230, the product equals the percentage of the sugar contained in the urine. Comparative estimation with other methods has shown that a difference in density of B corresponds to a sugar-content of 0.230 per cent.; consequently a difference in density of D will correspond to a sugar-content of D $\times$ 0.230 per cent. If a very accurate estimation is necessary, we must determine the temperature of the fluid before and after fermentation, and if they are not equal, must make a correction. If the temperature is higher after fermentation than before, one-third of a degree of the urinometer scale must be added to the specific gravity determined after fermentation for each degree of temperature. If the temperature after is lower than before fermentation, a similar deduction must be made. The urinometer should be very accurate, with subdivisions from

1000 to 1050, and sufficiently wide apart for careful reading, the urinometer glass of good size, so that the amount of urine is considerable. An excellent plan is to employ one urinometer for densities between 1000 to 1025, and a second for those between 1025 to 1050. Many authors have proved that this method is sufficiently accurate for clinical purposes (up to 0.1 per cent.), although it has been often questioned,[1] and certainly it is so simple as to be very practical for the ordinary physician.

The diminution in specific gravity can be determined directly without the use of a urinometer by weighing a measured quantity of urine upon an ordinary apothecary's hand-scale.

Quantitative Gas-volumetric Fermentation Test.—This method is based upon the fact that the amount of sugar in urine can be computed by measuring the volume of the carbon dioxid which is evolved by fermentation. To obtain useful results with this method, the volume of the carbon dioxid produced in the eudiometer tube must be read off with all the precautions necessary in gas-volumetric analyses, *i. e.*, with consideration of the barometric pressure, the temperature, the tension of the water vapor, the weight of the fluid shutting off the gas in the eudiometer tube, etc. The gas, too, must be measured inclosed in mercury, on account of the solubility of carbonic acid in water. The so-called self-fermentation of the yeast renders the accuracy very questionable, and, in any event, the process is too complicated for the ordinary practitioner. Einhorn's attempt to simplify the method for the practising physician the author regards as a failure.

Lohnstein's Accurate Fermentation Saccharometer.[2]—Lohnstein's accurate fermentation saccharometer is constructed upon manometric principles, measuring the pressure produced by the development of the carbonic acid. Its only disadvantage is that one of its parts cannot be regulated by the experimenter, who is consequently dependent upon the maker of the instrument. The author will omit a description of the saccharometer. It is easily used, and is praised by many authors as an accurate instrument. Wagner's precision fermentation saccharometer[3] is similar to that of Lohnstein in principle. It has the advantage that it is more easily cleaned.

The presence of protein in the urine does not in any way disturb the technic or accuracy of the fermentation tests. This is a great advantage, because with most other methods of determining the amount of sugar the urine must be first freed of protein.

Compressed yeast is employed so universally now throughout America that it seems hardly necessary to suggest any substitute.

POLARIMETRIC ESTIMATION OF GLUCOSE

The polarimetric estimation of glucose is probably the most convenient of all. It does, however, require a rather expensive apparatus, and it fails to estimate very small quantities. Almost any of the polariscopes are good enough, but the author especially recommends Wild's polaristrobometer. The principle, which is the same with all polariscopes, depends on the fact that a solution of glucose has the power to turn the plane of polarized light to the right. The angle of deflection is proportionate to the amount of sugar in the solution. It is known that when a ray of polarized light is taken up by an analyzing Nicol prism, the portion of light which passes through the analyzing Nicol varies decidedly according to the position of the Nicol relative to the plane of vibration of the polarized ray of light. If the plane of vibration of the analyzing Nicol is parallel to that of the polarized ray of light, the maximum amount of light will be transmitted; if at right angles to it, the minimum of light. If the position of the analyzing Nicol is now determined for this maximum or minimum, then the interposition of an optically active sub-

[1] Pflüger's Arch., 1884, vol. xxxiii, p. 211; 1885, vol. xxxvii, p. 479. Lohnstein, Berlin. klin. Woch., 1896, No. 6, p. 120.

[2] Allg. med. Centralzeit., 1899, No. 101; 1900, No. 30 *ff*.

[3] To be obtained from Götze, Fabrik für Glasinstrumenten, Leipzig.

stance, *e. g.*, a solution of glucose, will rotate the plane of the polarization of the ray of light with relation to the analyzing Nicol. Then, to determine again a maximum or minimum of light intensity, the Nicol itself must be rotated through a certain angle. The size of this angle will be proportional to the amount of the interposed substance, *e. g.*, sugar; this amount can, therefore, be calculated from the angle through which it is necessary to rotate the Nicol to produce the maximum or minimum of light. All polariscopes constructed for quantitative analysis depend upon this principle. Their only differences depend upon the employment of various optical contrivances in order to facilitate the determination of the position of the planes of vibrations to each other, *e. g.*, the interposition of doubly refracting bodies, peculiarly ground plates of quartz, etc. They produce peculiar optical appearances, according to the position of the Nicol, colors, stripes, etc.

Wild's instrument uses, as an indicator of the position of the planes of vibration, the system of parallel dark bands which, in a homogeneous polarized light (sodium flame), are made by two crossed quartz plates cut at an angle of 45° to the axis. The advantage of homogeneous light and parallel bands without color, which appear simply dark upon a light background, is that the test depends upon the examiner's sensibility to light alone, and not to color. The test with other instruments, *e. g.*, Soleil-Ventzke's, depends upon the sensibility of the eyes to color. Fig. 243 shows Wild's instrument. The analyzing Nicol prism and the quartz plates are set in the tube *a c*, and the polarizing Nicol prism in the tube *d e*. In looking through the instrument in a dark room, from *a* to the sodium flame at *b*, with the Nicols parallel and crossed, the parallel bands will appear upon the bright background of the field of vision (Fig. 243, IV). If one of the Nicols is rotated 45° by means of the screw *f*, the bands will disappear; further rotation will bring them back.

It should be noted that Pfister and Streit, of Bern, are now supplying Wild's instrument with a number of marked improvements which increase its accuracy, and make it possible, by employing the so-called half-shadow principle, to use a non-homogeneous strong light, and under some circumstances to omit entirely decolorizing the urine.

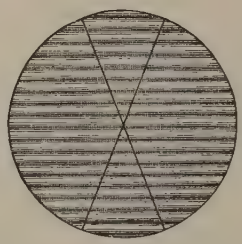
To estimate the amount of glucose by polarization, 50 cc. of urine are decolorized by shaking with about $\frac{1}{6}$ of this volume of the best animal charcoal and then filtering. If the urine is dark-colored, it must sometimes be allowed to stand for several hours with the animal charcoal, during which time it is frequently shaken; or it may be necessary to boil the urine containing the charcoal for a brief period. The decolorization should be complete. As Späth fears that some of the glucose may be absorbed by the charcoal, he recommends the following method of Patéin and Dufau for decolorization of the urine: A solution of mercuric nitrate is prepared by dissolving 200 gm. of acid nitrate of mercury in 500 to 600 gm. of water, and sodium hydroxid is added until a slight precipitate results. Sufficient water is added to bring the quantity up to 1 liter, and the mixture is filtered. Small quantities of this solution are added to 50 cc. of urine until no further precipitation occurs; a dilute solution of sodium hydroxid is added drop by drop until the reaction of the mixture is neutral or, at most, feebly alkaline; the quantity is brought up to 100 cc. by adding sufficient water, and the mixture is filtered. No precipitate should be produced by the addition of sodium hydroxid to the filtrate.

With urines which are not too deep in color, a Welsbach light may be used and the white light filtered through a glass cell 1 to 2 cm. thick, containing a 4 per cent. solution of potassium bichromate. This is placed between the source of light and the polarizer. In this way the preliminary decolorization may be avoided. With such a source of light the examination may be carried on in daylight, or daylight may be used as the source of light itself.

A metal tube (200 mm. long) (Fig. 243, II), which can be closed at both ends with parallel plain glass disks and metal caps, is filled with the decolorized urine. We must be careful not to include any air-bubbles, and not to press the glass plates by screwing the metal caps too hard, because under pressure the glass becomes doubly refractive, and the dark bands will not disappear with any position of the Nicol. When so arranged, the tube will contain a layer of urine exactly 200 mm. thick. The instrument is adjusted with a sodium flame in a dark room so that the parallel bands absolutely disappear, and the tube which contains the urine is then set upon the rest *c*, *d*. If the urine contains sugar, the bands will immediately reappear. They are then made to disappear by rotating the polarization plane with the polarizing Nicol by means of the screw *f*. At the moment when they disappear, the size of the angle through which the Nicol prism has been rotated is read off through the telescope *g h*, upon the scale *i*, by means of the vernier *k*. The gas-flame at *l*

I

II



IV

III

Fig. 243.—Wild's polaristrobometer.

serves to illuminate the scale. When the amount of sugar contained is very great, the tube III is substituted for tube II. In the latter, one of the parallel glass disks is placed at *M*, so that the thickness of the urine is *M m*—*i. e.*, 100 mm. The part *M o* is simply an empty continuation of the tube necessary for its adjustment. The angle of rotation is read off and the amount of sugar in tenths of 1 per cent. calculated directly from the following table:

Angle of rotation.	Thickness of urine layer, 100 mm. (length of tube).	Thickness of urine layer, 200 mm. (length of tube).
1 degree	1.984 per cent. glucose.	0.992 per cent. glucose.
2 degrees	3.968 " "	1.982 " "
3 "	5.952 " "	2.976 " "
4 "	7.936 " "	3.968 " "
5 "	9.920 " "	4.960 " "
6 "	11.904 " "	5.952 " "
7 "	13.888 " "	6.944 " "
8 "	15.872 " "	7.936 " "
9 "	17.856 " "	8.928 " "
10 "	19.840 " "	9.920 " "

The scale of the instrument is not graduated in minutes and seconds, but in tenths of degrees. Hence, the figures in the above table indicating the amounts of sugar corresponding to each degree can be used directly to express the amounts of sugar corresponding to tenths of degrees by simply moving the decimal point one place to the left. If, for instance, 3° rotation with a layer 100 mm. thick corresponds to 5.952 per cent. of glucose, then 0.3° will correspond to 0.5952 per cent. The calculation then becomes extremely easy, *e. g.*, if the rotation equals 3.2°,

$$\begin{array}{l} 3.0^\circ = 5.952 \text{ per cent.} \\ 0.2^\circ = 0.3968 \quad \text{"} \\ \hline 3.2^\circ = 6.3488 \text{ per cent.} \end{array}$$

The polarimetric estimation of the percentage of sugar can be, therefore, very speedily performed. A number of instruments constructed for clinical purposes give the results directly in percentages of glucose. They have the disadvantage that they are less convenient when one wishes to estimate the amount of β-oxybutyric acid or other substances polarimetrically.

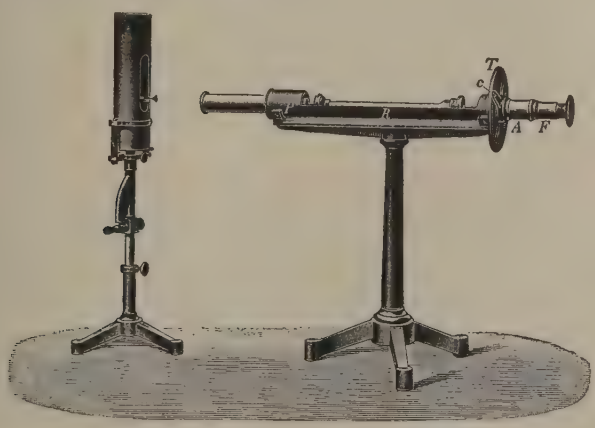


Fig. 244.—Simple polarimeter of Schmidt and Haensch for determining the amount of glucose in the urine.

Proteins, contrary to glucose, are levorotatory; hence, to obtain correct results with albuminous diabetic urine (see p. 566 et seq.), the protein must first be removed. Polarimetric estimation of sugar is accurate to about 0.5 per cent., which suffices

for all practical purposes, although results by means of the areometric fermentation test have a still narrower limit of error. With the polarimetric method, mistakes

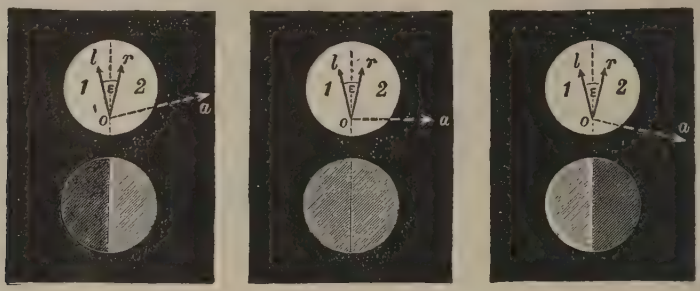


Fig. 245.—The half-fields of the Schmidt and Haensch apparatus. The center one shows the two fields alike, and is the point at which the apparatus is read for the amount of glucose.

are apt to occur, due to the occurrence in the urine of levogyrate substances (fructose, combined glycuronates, and β-oxybutyric acid).

[The instrument which is figured here (Fig. 246) is used extensively in America for the determination of sugar in the urine. It is simple in construction and not so

Fig. 246.—New form of polarimeter tube which may be filled conveniently.

expensive as the more complicated apparatus. The amount of glucose is given directly in per cent.—C. G. L. W.]

QUANTITATIVE DETERMINATION OF UREA

Normal human urine contains up to 4 per cent. of urea. The average amount of urea excreted in twenty-four hours[1] for a man on a mixed diet is about 33 gm., varying between 24 and 40, with starvation and non-nitrogenous diet, 15 to 20 gm. Women excrete from 20 to 32 gm. Upon a very rich protein diet even as much as 100 gm. has been excreted. Quantitative estimations of urea are most essential in all metabolic investigations.

The urea estimation may also be used to test the capability of complete digestion, *e. g.*, a very rich protein diet is ingested for one day by an individual in a condition of approximate nitrogenous equilibrium. We then estimate the total amount of urea for that day and the day following, and determine whether it is excreted in an amount proportionate to the ingested food. By far the greater part of the nitrogen introduced in the form of protein is eliminated as urea, and at most only a small amount of protein will be stored up in one day; hence, nearly the whole of the ingested nitrogen must appear as urea in the urine of the particular day, and perhaps of the following, provided protein food has been well utilized.

Following the suggestion of F. Hirschfeld, a patient ingests during one day a test-diet of 500 gm. of meat (106.25 gm. of protein), 8 eggs (48 gm. of protein), and 200 gm. of bread (18 gm. of protein), or a total of 172.25 gm. of protein. If the protein is well utilized, the patient will excrete at least 59 gm. of urea (27.5 gm. of nitrogen). If he does not excrete as much as that, the utilization is incomplete. Hirschfeld considers such a condition of insufficient utilization characteristic of certain cases of diabetes mellitus, and is inclined to attribute it to some functional disturbance of the pancreas. As a consequence of the slight elimination of urea, such cases are usually supposed not to present any increase in the quantity of urine.

[1] Vierordt, Daten und Tabellen, 1888.

APPROXIMATE ESTIMATION OF THE AMOUNT OF UREA BY MEANS OF THE SPECIFIC GRAVITY OF THE URINE

Urea affects the specific gravity of urine more than any other constituent; hence the specific gravity of the urine will furnish an approximate measure of the amount of urea, provided, of course, that sugar is absent. Experience has shown that a specific gravity of 1014 corresponds to about 1 per cent. of urea; of 1014 to 1020, to about 1.5 per cent.; of 1020 to 1024, to about 2 and 2.25 per cent.; of 1028, to about 3 per cent. This estimate must be modified in fever and in cachexia, in both of which the chlorid excretion is diminished.

If sugar is present, it must first be removed by fermentation before we can judge of the amount of urea from the specific gravity. In such an event it is better at the same time to employ the areometric method for the estimation of sugar (p. 623 et seq.), and then to recalculate the specific gravity found after fermentation, since the alcohol lowers this to some extent. The degree in which the specific gravity is thus lowered can be best determined by calculating the amount of alcohol from the result of the areometric estimation of sugar. Remembering that approximately equal amounts by weight of alcohol and carbon dioxid are produced in the fermentation of glucose, and having already determined the percentage of glucose, we can easily get the amount of alcohol in the fermented urine, for it will equal about half the amount of sugar found, *e. g.*, after fermentation, approximately a 1.5 per cent. solution of alcohol will result from a diabetic urine containing 3 per cent. of glucose. According to Hirschfeld,[1] the following specific gravities apply to watery solutions of alcohol at 15° C. (water = 1000): 1 per cent., 998.5; 2 per cent., 997; 3 per cent., 995.6; 4 per cent., 994.2. The specific gravity of the urine is thus diminished about 1.5 for every per cent. of alcohol in solution. Therefore, the specific gravity of the fermented urine must be increased by 1.5 for every per cent. of alcohol contained before we can estimate the urea by the above method.

LIEBIG'S METHOD FOR UREA BY TITRATION

Liebig precipitates the urea, in the form of urea mercuric nitrate, by means of a solution of mercuric nitrate. In its original form the method is very simple and convenient, but unless performed very carefully, many errors may arise, and even with the greatest care a number of corrections should be made. On account of these difficulties several modifications have been suggested, all of which furnish better results, but which are more complicated and require more technical skill than the original process. As a matter of fact, moreover, Liebig's method has been abandoned because it does not estimate the amount of urea in the urine, but rather the approximate amount of total nitrogen. (See p. 635.)

KNOP-HÜFNER'S METHOD OF ESTIMATING THE UREA

This is the simplest of all methods. It is to be used for clinical purposes. It depends upon the decomposition of urea into carbon dioxid, water, and nitrogen by means of a solution of sodium hypobromite in an excess of sodium hydroxid. The nitrogen liberated from a definite amount of urine is measured volumetrically, and from this the corresponding amount of urea is calculated. The carbon dioxid is absorbed by the excess of sodium hydroxid. For very accurate analysis the barometer and temperature must be considered. Other nitrogenous constituents of the urine (uric acid, kreatinin, etc.), and especially ammonia, are partially broken up at the same time, liberating nitrogen; hence the method is not absolutely accurate. According to Emerson, about 8 per cent. of the urea is not changed to carbon dioxid and nitrogen. Hence, one obtains a compensating error. Both are not large. If a diabetic urine be examined, a relatively large error may be encountered, owing to the presence of much ammonia. This may be avoided by making the urine alkaline with sodium hydroxid, and removing the free ammonia with a current of air. Proteins evolve nitrogen with sodium hypobromite. They should be removed before the estimation is performed.

[1] Zeit. f. klin. Med., 1891, vol. xix, p. 338.

Hüfner's apparatus, represented in Fig. 247, has been modified again and again to more or less advantage. It consists of three separate parts:

1. The dilated glass receptacle, *C*, connected by means of a ground-glass stopper with a smaller one, *D*, which holds from 6 to 7 cc.

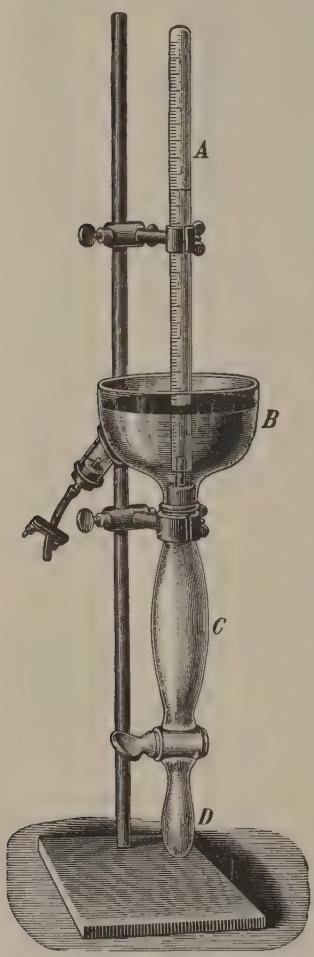


Fig. 247.—Hüfner's apparatus for estimation of the urea.

2. The bell-shaped glass vessel, *B*, open at both ends, and connected with the upper end of *C* by means of a perforated hard-rubber stopper.

3. The eudiometer tube, *A*, divided into centimeters and fractions, to be placed when in use within vessel *B* over the upper end of *C*.

Preparation of the sodium hypobromite solution: 70 cc. of a 30 per cent. sodium hydroxid solution are mixed with 180 cc. of water and 5 cc. of bromin. The latter dissolves with the formation of sodium bromid and sodium hypobromite.

$$2\ NaOH + Br_2 = NaBrO + H_2O + NaBr.$$

As soon as the bromin has dissolved, the reagent is ready for use. It should be freshly prepared every day or two, because the hypobromite gradually becomes decomposed. It should also be kept in a cool, dark place—best of all, in an ice-chest—and never employed when warm from mixing.[1]

Technic of the Method.—The amount of urea in the urine to be examined is first approximately estimated by the specific gravity (p. 629 et seq.), and then, if necessary, the urine is diluted so that the amount of urea present is not above 1 per cent. Five cc. of the urine, or of a diluted portion (when necessary), are removed in a long, thin pipet and allowed to run into the vessel *D*, carefully avoiding wetting the sides of *C*. In the same pipet is then sucked up 1 to 2 cc. of water, in order to remove any urine adhering to its sides. The receptacle *D* is then filled with the contents of the pipet exactly to the upper margin of the bore in the glass stop-cock. This is now shut off. Then the vessel *C* is filled to overflowing with the hypobromite solution, and next the vessel *B*, as well as the eudiometer tube, is filled with concentrated sodium chlorid. The tube is inverted over the opening of the vessel *C* under the level of the liquid in *B*, its opening having been first closed with the thumb, and the inclusion of air avoided. *A* is now held in position by the retort stand, which also supports the other parts. Now, as soon as the stop-cock is opened, the heavy hypobromite solution in *C* becomes mixed with the lighter urine in *D*, and nitrogen develops actively. This gas accumulates in the eudiometer tube, gradually displacing the salt solution. The decomposition is complete in from twenty

[1] [The method of preparation of the hypobromite solution as outlined by Rice can be highly recommended. Two solutions are necessary, and may be retained for any ordinary length of time:

1. A solution of 125 gm. of bromin and 125 gm. of sodium bromid in sufficient water to make the volume up to 1000 cc.

2. A solution of sodium hydroxid of a specific gravity of 1250 (22.5 per cent.). To prepare the hypobromite for use, mix equal volumes of the two solutions, and dilute with 1½ volumes of water.—Ed.]

minutes to one-half hour. The bubbles adhering to the sides of the vessel are then gently shaken into the eudiometer tube, which is closed under the level of the salt solution with the thumb. It is then removed, and submerged as completely as possible, opened downward, in a large cylinder filled with water at the room temperature. After about fifteen minutes the eudiometer tube and its contents will be at the same temperature as the surrounding water. The tube is then lifted far enough out of the water to equalize the levels of the fluid inside and outside, and at this moment the volume of the inclosed nitrogen is read off. The temperature of the water and the barometric pressure should also be recorded. The volume of gas estimated must now, for the purpose of calculation, be reduced to 0° C., 760 mm. barometric pressure, and absolute dryness, according to the formula:

$$v^1 = \frac{v\,(b - w)}{760\,(1 + 0.00366\,t)}$$

v^1 = Reduced volume desired.
v = Volume read off.
b = Barometric pressure at the time of reading, in mm. Hg.
w = Tension of water vapor at a temperature t, in mm. Hg.
t = Temperature of water at time of reading.
0.00366 = Coefficient of expansion of gases for 1° C.

The values for w corresponding to the temperatures usually met with are as follows:

10° C.	9.126	18° C.	15.351
11° C.	9.751	19° C.	16.345
12° C.	10.421	20° C.	17.396
13° C.	11.130	21° C.	18.505
14° C.	11.882	22° C.	19.675
15° C.	12.677	23° C.	20.909
16° C.	13.519	24° C.	22.211
17° C.	14.009	25° C.	23.582

One gm. of urea furnishes 354.3 cc. of nitrogen (a little less than the theoretic quantity); hence, the following proportion will determine the amount of urea (x) in the 5 cc. of urine employed.

$$354.3 : 1 = v' : x$$
$$x = \frac{v'}{354.3} \text{ gm.}$$

The percentage of urea contained in the urine can be very easily determined by multiplying this number by 20. Of course, if the urine was diluted before the estimation, this dilution must also be considered.

The author considers that Gerrard's[1] improvement upon Hüfner's apparatus has been shown to be the most practical for the practitioner (Fig. 248).

A graduated glass tube, a, fixed in a wooden stand, is connected at the lower end by means of a side projection and a rubber tube with a vessel, b, which is open at the top, and at its upper end with a wide-necked bottle, d, by means of a perforated rubber stopper, c, and a rubber tube. Vessel b may be raised or lowered upon the graduated tube by the metal spring clamp e. The wide-necked bottle, d, is filled with 100 cc. of sodium hypobromite solution; 5 cc. of urine are poured into the small test-tube, f, which is carefully placed in bottle d, so as to be, for the time being, protected from the hypobromite solution. The bottle is then connected with the rest of the apparatus by means of the perforated rubber stopper g and tube gh. Next, the stopper c is removed and vessel a is filled with water up to the zero mark of the scale. Of course, the communicating vessel b, which has been pushed up toward the top, also fills to the same level. The stopper c is now replaced. While this is being done, the spring clamp i, which closes the rubber tube attached to the glass tube h, is opened carefully so that at the moment of replacing c there will be no increase of pressure of the air upon the level of the water. The fluid, therefore, remains at the same level in the communicating vessels a and b. The spring clamp i is now very carefully closed again. After the apparatus has been connected in this fashion, the urine in the little glass f is easily

[1] Lancet, 1884, ii, p. 952.

poured out into the bromin solution by repeatedly tipping the vessel *d*. The development of gas follows immediately. Bottle *d* is placed in a large vessel of water at the room temperature (15° C.), while the development of gas continues. To make it sink, the bottle is furnished with a lead framework, as shown in the picture. The object of having the gas develop under water, at the temperature of the room, is to distribute the heat which arises as the result of the chemical reaction of the hypobromite solution. This heat will not only influence the decomposition, but will also increase the volume of the liberated nitrogen gas. We need not correct the gas volume, since both the gas and the apparatus may be considered to be at the room temperature of 15° C. The nitrogen set free accumulates in the upper part of the graduated tube *a*, gradually elevating the level of the water in *b*. The evolution of the gas may be materially hastened by gently shaking the bottle *d*. When the

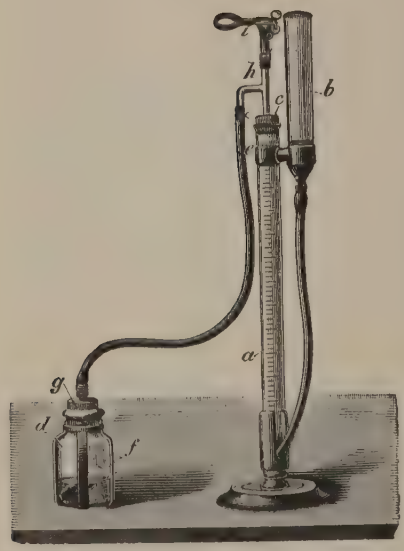


Fig. 248.—Gerrard's apparatus for estimation of urea.

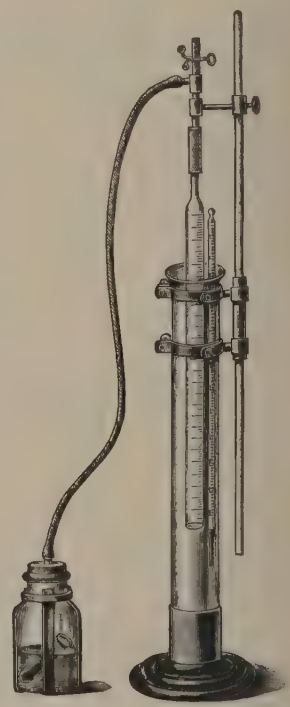


Fig. 249.—Dupré's apparatus for estimating urea.

decomposition is complete, the gas can be put under ordinary atmospheric pressure by lowering vessel *b* sufficiently to equalize the level of the fluid in *a* and *b* again. Then the volume of the nitrogen is read off.

The scale upon the English instrument indicates empirically the amount of urea at room temperature and normal barometric pressure (760 mm.). Mariotte's law can then be made use of to correct the reading according to the barometric pressure, viz.:

$$\frac{v}{v'} = \frac{b'}{b}.$$

v and b and v' and b' represent the corresponding gas volumes and barometric pressures. v and v' may be directly replaced by the amount of urea proportion-

ate to them, so that the formula then becomes, when h and b represent the amounts of urea corresponding to the barometric pressures,

$$\frac{h}{h'} = \frac{b}{b'}.$$

It is advisable to control the empirical scale by adding a scale in cubic centimeters on tube a. Then the calculation for any temperature or barometric pressure can be made in the same manner as with Hüfner's apparatus. (See p. 630.) The same rules for dilution, of course, apply for this apparatus as for Hüfner's.

Not only is Gerrard's instrument more compact than Hüfner's, but the gas can be entirely evolved within a few moments by shaking bottle d.

The weak point of the apparatus is the closure of the upper end by a stop-cock, which may easily allow of the escape of gas, and consequently give rise to an erroneous result. Dupré's modification of Hüfner's apparatus (Fig. 289) can be thoroughly recommended, and is the one which is employed in the author's clinic. The illustration should be sufficient without further description. It differs from Gerrard's apparatus in that the reduction of the gas to atmospheric pressure is accomplished by moving the buret in which the gas collects, and which is suspended in a cylinder filled with water. In this instrument the stop-cock at the upper end of the buret should be carefully tested, in order to avoid losing any of the gas.

Table giving the amount of urea in grams for each cc. of nitrogen evolved in the Knop-Hüfner method.

According to Seiler and Ratschy (Schweiz. Woch. Pharmacie, 1889, No. 46) the intermediate values for temperature between these given in the table may be interpolated. They are given in full in the original table of Seiler and Ratschy:

Barometric pressure in millimeters of mercury.	Temperature in degrees Centigrade.			
	5°	10°	15°	20°
700	0.002490	0.002434	0.002377	0.002321
705	0.002505	0.002451	0.002394	0.002339
710	0.002522	0.002468	0.002412	0.002355
715	0.002542	0.002487	0.002430	0.002373
720	0.002559	0.002504	0.002447	0.002389
725	0.002578	0.002523	0.002464	0.002405
730	0.002595	0.002540	0.002482	0.002423
735	0.002614	0.002559	0.002499	0.002440
740	0.002631	0.002576	0.002517	0.002457
745	0.002647	0.002591	0.002534	0.002474
750	0.002665	0.002609	0.002551	0.002491
755	0.002683	0.002626	0.002568	0.002508
760	0.002701	0.002644	0.002586	0.002525

ESTIMATION OF UREA BY SCHÖNDORFF'S METHOD

The principle of this method is as follows: The urine is precipitated by phosphotungstic acid containing hydrochloric acid, during which the urea remains in solution. The filtrate is then heated with phosphoric acid, ammonium phosphate is formed, and the ammonia is freed from this compound by the addition of caustic soda. The ammonia is then removed by distillation and determined by titration, as in Kjeldahl's method (see below).

As the opinions in reference to the value of this method are still very contradictory,[1] it will suffice to refer the reader to the original work of Schöndorff (Pflüger's Arch., vol. lxii); to v. Jaksch (Klin. Diagnostik innerer Krankheiten, fifth ed.); to Pfaundler (Zeit. f. physiol. Chemie, 1900, vol. xxx), and to Folin (ibid., 1901, vol. xxxii).

[1] See Späth, Die chemische u. mikroskopische Untersuchung des Harnes, second ed., 1903.

QUANTITATIVE ESTIMATION OF UREA ACCORDING TO FOLIN[1]

This method is based on the fact that urea, when boiled with saturated solutions of magnesium chlorid, is converted into ammonia.

Five cc. of urine, 20 gm. of crystalline magnesium chlorid, and 2 cc. of hydrochloric acid are placed in a flask, closed with a reflux condenser of the shape given in Fig. 250. The mixture is heated on an electric stove for an hour and a half, the heat being greatest at the beginning, and reduced toward the end of the reaction. The heat is so regulated that drops of liquid falling from the condenser produce a marked hiss when they fall upon the contents of the flask. On cooling, the contents of the flask are diluted with 500 cc. of distilled water, and transferred quantitatively to a distilling flask. Ten cc. of 20 per cent. sodium hydroxid, a small amount of talcum, and a small piece of paraffin are added. The distillate is caught in a definite volume of standard sulphuric acid, and finally titrated with alkali as in the Kjeldahl method. As the magnesium chlorid is practically never free from ammonia, a control estimation must be made to ascertain the ammonia contained in 20 gm. The preformed ammonia must also be estimated, and subtracted from that of the total ammonia found by Folin's method. This may be done by the methods of Shaffer or Folin.

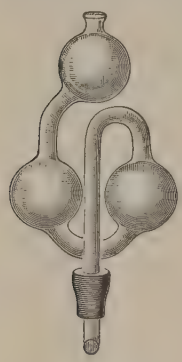


Fig. 250.—Reduced to about $\frac{2}{15}$ original size.

[**Methods for Determining Urea.**—Until recently the only method which has been used by the clinician for the determination of urea was some modification of the hypobromite test. It has long been recognized by those engaged in a more accurate study of the urine that this method in any of its most varied forms is entirely inadequate for any practical purpose. It still occupies a prominent place in text-books of clinical chemistry. The reason that it fails to estimate the amount of urea in the urine is a fundamental one, and cannot be obviated by any form of apparatus. Urea is not completely decomposed by sodium hypobromite in the concentrations occurring in the urine, and a number of substances constantly occurring in this fluid, such as ammonia, kreatinin, and substances entering into the group of undetermined nitrogen are partly decomposed. The reason why the determination sometimes gives results agreeing with the more accurate methods is that the two errors may compensate one another.

Only two methods at the present time fulfil the conditions for the accurate estimation of the urea nitrogen. These are the methods of Morner-Sjöqvist and of Folin. The latter method is finding its way more and more into clinical laboratories, and it seems fair to assume that this method, or some modification of it, by which it may be simplified, will be adopted for general clinical use.—C. G. L. W.]

[1] Zeit. f. physiol. Chem., xxxii, p. 505; xxxvi, p. 333; xxxvi, 548.

ESTIMATION OF THE AMOUNT OF TOTAL NITROGEN IN THE URINE BY KJELDAHL'S METHOD

Approximate values for the amount of total nitrogen in the urine may be obtained from the estimation of the amount of urea (Knop-Hüfner's method).[1] In the calculation we must assume that 15 parts of urea contain 7 parts of nitrogen, and in this calculate the amount of nitrogen belonging to the urea present. This amount must then be multiplied empirically for normal urine by 1.136, and for fever urine by 1.18. This will approximately furnish the amount of total nitrogen excreted.

Liebig's method, the so-called urea titration, also approximately estimates the amount of total nitrogen. The figures found for the quantity of urea by this method are too high, so that, in fact, the nitrogen obtained from the calculation of the urea supposed to be present really corresponds approximately to the total nitrogen contained in the urine.

For a perfectly exact estimation of the amount of total nitrogen in the urine, Kjeldahl's method is to-day almost exclusively employed. The principle of the method is that the organic constituents of the urine are destroyed by oxidation when the urine is heated with concentrated sulphuric acid, and that the nitrogen of those substances which do not contain it combined with oxygen appears as ammonium sulphate. The urea is changed directly into carbon dioxid and ammonia. The nitrogen is estimated by liberating the ammonia from the acid solution with potassium or sodium hydroxid, distilling it off, and passing it into a measured amount of acid. The acid remaining is then titrated with an alkali.

The details of the method, including certain modifications recommended by Wilfahrt and by Salkowski, are as follows; The acid used for oxidizing purposes is a mixture of 500 cc. of concentrated sulphuric acid and 100 gm. of phosphoric anhydrid. Pure sulphuric acid may be employed, but oxidation takes longer. It is also necessary to have a $\frac{N}{2}$ hydrochloric acid solution prepared by diluting the normal acid with an equal amount of water. A $\frac{N}{2}$ solution of sodium hydroxid is also essential.

Ten cc. of urine (or 5 cc. of concentrated) are put into a Kjeldahl flask with round bottom and long neck, to which are added 10 cc. of the sulphuric acid mixture, after about 0.4 gm. of finely divided mercuric oxid[2] has just been placed in the flask. This mercury acts catalytically in aiding oxidation. The flask is next loosely closed with a glass ball, and heated in a fume closet while kept somewhat tilted. The flame should not be too high and should be applied until the solution is colorless. Even the slightest tinge of yellow suggests that oxidation is not complete unless iron compounds are present in rather large quantities. As a rule, it takes at the most three hours to complete the oxidation. The mixture is now allowed to cool, and is poured into a distilling flask by means of a funnel. The digestion-flask and the round glass stopper are rinsed with 100 cc. of water, which is added to the contents of the distillation-flask. Next, 40 cc. of sodium hydroxid solution of specific gravity 1340 are added and (in order to precipitate the mercury, which otherwise would form amido-compounds with the ammonia) this is followed by 25 cc. of potassium sulphid solution (40 gm. to the liter). The flask is now *quickly* connected with the distilling tube. This tube passes through a condenser, and the end is placed in an Erlenmeyer flask of about 200 to 300 cc. capacity. This latter vessel contains 20 cc. of the $\frac{N}{2}$ hydrochloric acid, and just enough water to keep the end of the condenser tube submerged.

Distillation is continued until no more ammonia escapes and the distilled steam no longer develops ammonium chlorid fumes, when a glass rod, moistened with HCl, is held in front of the open end. This condition of affairs usually obtains when about 100 cc. of fluid have been obtained by distillation. Several drops of a methyl-orange or cyanin solution[3] are now added to the $\frac{N}{2}$ hydrochloric acid solution to act as indicator, and the amount of contained ammonia is determined by titration

[1] Cf. Anleitung zur qualitativen und quantitativen Harnanalyse, Neubauer und Vogel, Neubearbeitet von H. Huppert, 1890, p. 531.

[2] Instead of using mercuric oxid as a catalyzer, copper sulphate may be employed. The subsequent precipitation with potassium sulphid is avoided. The digestion is finished when the solution assumes a light greenish-blue color.

[3] Cochineal solution, prepared by extracting ground cochineal with 50 per cent. alcohol, is often employed. The indicator can be used with artificial light.

with an $\frac{N}{2}$ sodium hydroxid solution. The amount of nitrogen in the quantity of urine employed may then be calculated from the amount of ammonia. The number of cubic centimeters of $\frac{N}{2}$ sodium hydroxid solution used is deducted from 20 cc., and the difference, multiplied by 7.02, gives the number of milligrams of nitrogen in the quantity of urine employed.

This test is best performed with the commercial Kjeldahl apparatus, which permits the oxidation and distillation of a number of specimens at the same time. This shortens very much the amount of time necessary, especially as one is usually obliged to make a series of tests.

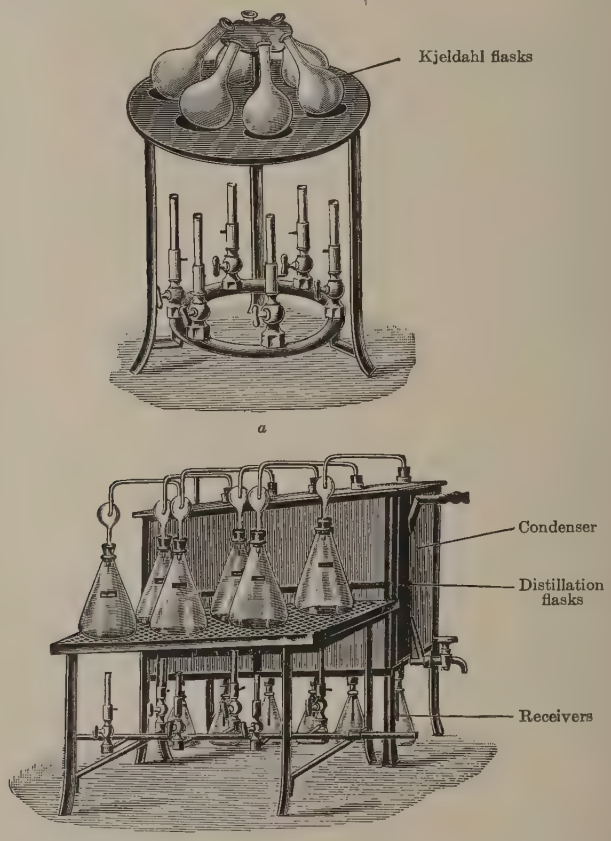


Fig. 251.—Kjeldahl's apparatus: *a*, Apparatus for the simultaneous oxidation of 6 specimens; *b*, apparatus for the simultaneous distillation of 6 specimens.

In this form the method is perhaps rather too complicated for clinical purposes; Henninger[1] and Schönherr's modification seems to be more convenient. The amount of ammonia produced by the destruction of the organic substances is estimated azotometrically, and the distillation is omitted, as in Knop-Hüfner's method of estimating urea. The ammonia is decomposed by sodium hypobromite solution, and liberated nitrogen is measured volumetrically.

[1] Compt. rend. de la soc. de biol., 1884, p. 474; Jahresbericht f. Thierchemie, 1884, p. 205. O. Schönherr, Chemikerzeitung, xii, 217; Chem. Centralbl., 1888, p. 420.

The technic for the procedure is as follows: After the oxidation of 5 to 10 cc. of urine, according to the method given above: Instead of using mercuric oxid or copper sulphate, Denigès employs 5 cc. of a 30 per cent. neutral potassium oxalate as a catalyzing agent. The former compounds combine with the ammonia. The solution is diluted with a little water, and partially neutralized with potassium or sodium hydroxid until the reaction is only faintly acid, and then the volume made up to 50 cc. For azometric analysis we use 20 cc. (corresponding to 2 or 4 cc. of urine) of this solution and treat it exactly like the urine in Knop-Hüfner's method (p. 629), although, of course, the size of the apparatus must be changed somewhat. With Gerrard's or Dupré's modification this can be accomplished very simply by selecting a tube (Figs. 248 and 249) which will contain 20 cc. instead of 5 cc.

The total elimination of nitrogen in the urine generally runs parallel to the urea excretion, which, of course, contains the greater share of the nitrogen. In acute yellow atrophy of the liver, however, the comparison of the total amounts of nitrogen and of urea elimination shows a strikingly different result. In this disease the major portion of nitrogen is eliminated as leucin and tyrosin, and little or no urea is excreted in the urine. In diabetic acidosis a large amount of the nitrogen may be excreted in the form of ammonia.

QUANTITATIVE ESTIMATION OF URIC ACID

A healthy adult excretes 0.2 to 1 gm. of uric acid in the urine during the course of twenty-four hours. The amount increases physiologically with increased ingestion of food, and pathologically with increased metabolism of nitrogen in about the same proportion as urea. The amount of uric acid in normal urine varies with its specific gravity. The last two numbers of the specific gravity (calculated to 4 places) multiplied by 2 gives approximately the number of centigrams of uric acid in the liter. The daily excretion of uric acid is pathologically increased in fever, in leukemia, and in cirrhosis of the liver. Opinions still differ about uric-acid excretion before, during, and after attacks of gout. Recent investigations probably disprove the old theory—that in gout more uric acid is permanently produced than normally (so-called uric-acid diathesis). According to Haig, the amount of uric acid formed in the body bears a constant ratio to the amount of urea (1 : 35 both under physiologic and under pathologic conditions—*e. g.*, even in gout). He claims that variations in this ratio are due chiefly to irregularities of elimination. This seems to be not altogether proved. Again, the elimination of uric acid will be increased, *ceteris paribus*, by the ingestion of uric acid and other xanthin bodies, as well as by food substances rich in nuclein (rich in cell nuclei).

According to Grübler,[1] the amount of uric acid in the urine may be approximately estimated by stratifying upon a layer of nitric acid a specimen of urine in a test-tube, so that the volume of urine shall be to the volume of acid as 3 : 2. After a short interval uric acid will precipitate out as a cloudy ring at the junction of the two fluids. If the amount of uric acid is increased, the precipitation will be plain within five minutes; if diminished, not until later. Of course, this test applies only when the daily volume of urine is normal. If the volume is diminished, the urine must be diluted up to the normal amount with water. Albuminous urine must first be freed from protein by boiling, after slight acidification.

Heintz's quantitative method of estimating the amount of uric acid has been abandoned entirely. It is not trustworthy. The following three methods are, however, quite accurate:

[1] Laquer, Schmidt's Jahrbücher, 1892, vol. ccxxxvi, No. 10, p. 78.

THE LUDWIG-SALKOWSKI METHOD OF ESTIMATING THE AMOUNT OF URIC ACID

This method gives the most accurate results in the estimation of uric acid. The principle is as follows:

Uric acid, even if present only as a trace, will be precipitated from the urine as silver urate upon the addition of a mixture of a solution of ammoniacal silver nitrate and of ammoniacal magnesia solution. The precipitate is treated with an alkaline sulphid solution and so decomposed. Silver sulphid and ammonium urate will be formed; the latter is filtered off. The uric acid separates from the solution upon evaporation with hydrochloric acid, and is then dried and weighed.

The precipitation of uric acid by the addition of ammoniacal magnesia solution has, aside from the advantage of the slight solubility of the double combination of urate, the additional advantage that triple phosphate is precipitated, at the same time mixing with the otherwise gelatinous urate precipitate and making it less tenacious and more easy to be washed.

For the procedure, the following solutions must be prepared:

1. Ammoniacal silver solution: 26 gm. of silver nitrate are dissolved in distilled water, and enough ammonia added to the solution to redissolve the precipitated silver oxid. The mixture is then diluted with water up to 1 liter.

2. Ammoniacal magnesia solution: 100 gm. of magnesium chlorid are dissolved in water. About 200 cc. of a cold saturated ammonium chlorid solution are added, and then enough concentrated ammonium hydroxid to give the mixture a strong ammoniacal odor. This mixture contains a double salt of magnesium chlorid and ammonium chlorid, which is not precipitable by ammonia. The mixture is diluted with water up to 1 liter.

The solutions as given in Ludwig's directions are of such concentration that 10 cc. will suffice for 100 cc. of urine.

Ten cc.[1] of the silver solution are mixed with 10 cc. of the magnesium solution, and the resulting precipitate of silver chlorid is redissolved by the addition of ammonium hydroxid. If the precipitate does not dissolve perfectly, it must contain magnesium hydroxid, which can be dissolved by adding ammonium chlorid. The clear solution is poured, with stirring, into a beaker containing 100 cc. of urine; the precipitate which forms is allowed to settle a little, then filtered off upon a suction filter, and washed two or three times with water to which a few drops of ammonia have been added. Any of the precipitate remaining in the beaker is washed out into the filter with wash-water. Traces of the precipitate may, however, be allowed to remain in the beaker, because all the precipitate on the filter is to be removed, by the aid of a glass rod, to the beaker again, after it has become partly dry on the paper. The filter-paper must be kept intact.

The precipitate is now placed in about 200 cc. of water, according to Salkowski, acidulated with hydrochloric acid, and the mixture saturated with hydrogen sulphid. Shaffer and Folin recommend the previous addition of 5 to 10 cc. of a 1 per cent. solution of cupric sulphate, after which the fluid is brought to the boiling-point. After the saturation with hydrogen sulphid, the fluid is again boiled for several minutes, and the hot solution of uric acid is then filtered from the silver sulphid. The precipitate should be thoroughly washed with hot water. The filtrate is perfectly clear and throws down no silver sulphid upon evaporation, just as in Ludwig's method, in which the silver is removed by an alkaline sulphid solution. The fluid is now placed in a porcelain dish upon a water-bath, and evaporated to 10 to 15 cc. From 5 to 10 drops of hydrochloric acid are now added, the mixture is allowed to stand for twelve hours, and the uric-acid crystals are collected upon a weighed filter which has been dried at 110° C. The crystals upon the filter are then washed with a small quantity of water until they are free from chlorin; the quantity of the filtrate, together with that of the wash-water, should not exceed 50 to 60 cc. The crystals are again washed twice with absolute alcohol, then with ether, dried, and weighed.

Any sediment of urates must be dissolved by heating before measuring off the urine. Any precipitated uric acid can be dissolved in as little sodium hydroxid as possible and the solution then mixed with the urine. Too much sodium hydroxid should not be used, for it would cause excessive precipitation of phosphates, which would not allow any phosphate to remain for the production of a triple phosphate

[1] The following description is partly quoted from Huppert: Anleitung zur qualitativen und quantitativen Harnanalyse von Neubauer, Neubearbeitet durch Huppert, 1890.

sediment with the silver magnesium precipitation. Adding sodium phosphate to the urine before the silver precipitation would, however, prevent this difficulty.

Stadthagen claims that peptones and proteoses do not influence the uric acid precipitation, but the urine must first be freed from albumin.

THE HOPKINS-WÖRNER METHOD OF URIC-ACID ESTIMATION[1]

This method is, according to all observers, simple and perfectly accurate. It depends upon the following principle: Ammonium chlorid precipitates uric acid quantitatively from the urine as ammonium urate. The determination is carried out as follows: 150 cc. of urine are warmed in a beaker to 40° to 45° C., and 30 gm. of ammonium chlorid allowed to dissolve in it. The precipitate of ammonium urate which results after one-half to one hour's standing is filtered off, and washed free from chlorin with a 10 per cent. solution of ammonium sulphate. It is then dissolved upon the filter by a warm 1 to 2 per cent. solution of sodium hydroxid, the filter washed afterward with hot water, and the filtrate and wash-water, collected in a porcelain dish, heated upon a water-bath long enough to drive off all the ammonia. The alkaline solution of uric acid is then decomposed with 15 cc. of concentrated sulphuric acid and some copper sulphate.[2] After adding sodium hydroxid, the free ammonia is estimated in the usual manner. Such a small amount of ammonia is more accurately measured by employing a $\frac{N}{10}$ oxalic acid instead of a $\frac{N}{2}$, as is usual, and also by retitration. One cc. $\frac{N}{10}$ oxalic acid corresponds to 0.0042 gm. of uric acid. Strongly acid urines under some conditions prevent the precipitation of ammonium urate, or make such a precipitation incomplete; hence, Levandowski[3] recommends that the urine be neutralized before the precipitation. If performed in this way, the method should be very exact and trustworthy.

KOWARSKI'S MODIFICATION OF HOPKINS' METHOD

A. Kowarski has modified the above method for clinical purposes.[4] Ten cc. of urine are measured out accurately into a centrifuge tube holding 15 cc. Two or 3 drops of ammonium hydroxid solution and 3 gm. of powdered ammonium chlorid are added. The tube is closed with a rubber stopper and shaken until the ammonium chlorid is dissolved. Ammonium urate is precipitated in the form of a flocculent sediment. The phosphates which are precipitated at the same time do not interfere with the estimation. The tube is allowed to stand for two hours. The mixture is then centrifuged for one to two minutes. The supernatant clear liquid can be poured off from the sediment without loss. This should be done at one time, as much shaking of the tube will disturb the sediment.

To the sediment 5 drops of concentrated hydrochloric acid are added, and the whole heated carefully over a small flame. The ammonium urate is dissolved, and the uric acid commences to separate out in the form of a crystalline precipitate. The separation is complete in one hour. Two cc. of water are added to the precipitate, the whole shaken, and again centrifuged. Ten revolutions of the centrifuge are sufficient completely to sediment the precipitate. The supernatant fluid is again poured off, and the precipitate washed at least three times with 2 cc. of alcohol, until the washings are neutral to litmus. The washing takes at the most three to five minutes. To the sediment are then added 2 cc. of hot water, 1 drop of phenolphthalein, and the mixture titrated with $\frac{N}{10}$ piperidin solution[5] prepared as given below. The titration is carried on until a permanent pink is obtained. The solution must be constantly shaken during the titration. If the number of cubic centimeters of piperidin solution used be multiplied by 3.36, one obtains the number of milligrams of uric acid contained in 10 cc. of urine. The piperidin solution is permanent. It can be controlled from time to time by titration against a standard solution of sulphuric acid. The piperidin solution is prepared[6] by dissolving more

[1] Wörner, Zeit. f. physiol. Chemie, vol. xxix, p. 1.

[2] This takes the place of the oxid of mercury (p. 635). It acts catalytically, and has the advantage that the subsequent treatment with alkaline sulphid becomes unnecessary.

[3] Zeit. f. klin. Med., 1900, vol. xl, pp. 3 and 4.

[4] Deut. med. Woch., 1906, No. 25, p. 497.

[5] Suggested by Tunnicliffe and Rosenheim.

[6] Huppert, Neubauer, und Vogel, Anleitung zur Analyse des Harnes, 10. Aufl., 1898, p. 815.

than the required quantity of piperidin in water, titrating with standard acid, and diluting to the proper volume. The amount required for 1000 cc. of water is 1.7 gm.

The method takes three and one-quarter to three and one-half hours. As the solution stands for three hours, only fifteen to twenty minutes are actually required for the determination.

If the urine contains undissolved uric acid or urates, a few drops of sodium hydroxid or sodium carbonate solution are added to dissolve them. In carrying out the estimation care must be taken to centrifuge the ammonium urate as completely as possible, so that it occupies as the minimum volume. The author found that the results were as accurate as those of Ludwig-Salkowski and Hopkins.

TITRATION OF URIC ACID, ACCORDING TO HOPKINS, MODIFIED BY O. FOLIN AND P. A. SHAFFER[1]

This method, suggested by Folin, differs from that of Hopkins-Wörner in that the ammonium urate is precipitated with ammonia and ammonium sulphate The precipitate is washed from the filter by 100 cc. of water. After the addition of 15 cc. of concentrated sulphuric acid, the solution is at once titrated with a $\frac{N}{20}$ potassium permanganate solution (1.6 gm. of crystalline potassium permanganate dissolved in water and the volume made up to 1 liter).

Folin and Shaffer found that the method gave high results with a number of urines, due to the fact that certain unknown substances were precipitated simultaneously with the uric acid and reduced the potassium permanganate. Folin and Shaffer have suggested a modification of the original method in adding the ammonium salt in acid solution with the addition of uranium acetate. The unknown substances are precipitated together with uranium phosphate. After filtration the mixture is made alkaline with ammonia, and the whole allowed to stand for twelve hours. The ammonium urate is precipitated and is titrated with potassium permanganate as above. The details of the method are as follows:

Five hundred gm. of ammonium sulphate, 5 gm. of uranium acetate, and 60 cc. of 10 per cent. acetic acid are added to 650 cc. of water. The whole occupies a volume of about 1000 cc. To 300 cc. of urine are added 75 cc. of the reagent. The mixture is allowed to stand for five to fifteen minutes, and filtered through a folded filter. Two portions of the filtrate of 125 cc. each are placed in two beakers. To each is added 5 cc. of ammonia, and stirred. The mixture is allowed to stand till the next day. The solution is then filtered through a Schleicher and Schüll filter No. 597, and the precipitate washed with 10 per cent. ammonium sulphate solution until it is nearly free from chlorin. The washing takes about twenty to thirty minutes. The precipitate is washed back into the beaker with hot water. Fifteen cc. of concentrated sulphuric acid are added and the solution titrated with $\frac{N}{20}$ potassium permanganate. The end-reaction is a faint rose color throughout the liquid. Toward the end of the reaction it is advisable to add the permanganate in portions of 2 drops at a time. The end of the reaction is observed when the rose color is seen throughout the liquid. It is not permanent. Each cubic centimeter of the permanganate solution corresponds to 3.75 mg. of uric acid. Pure permanganate solutions are quite stable, but may be controlled from time to time by titration against normal oxalic acid solution. If crystalline potassium permanganate (Kahlbaum) be used, the salt may be weighed out directly without control. Folin and Shaffer recommend a correction of +3 mg. of uric acid for every 100 cc. of urine used to make up for the solubility of the ammonium urate.

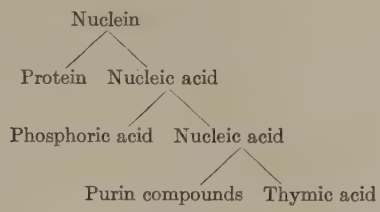
Toward the end of the titration the permanganate solution must be cautiously added drop by drop. The end-reaction is the first slight permanent reddish tinge obtained by stirring the fluid. The permanganate solution may be tested by a normal oxalic acid solution. One cc. of a $\frac{N}{20}$ permanganate solution corresponds to 0.00375 gm. of uric acid.

ESTIMATION OF THE ALLOXURIC OR PURIN BODIES IN THE URINE

Recent investigations concerning the relation of purin bodies (this word is now used to include uric acid and alloxuric or xanthin bases) to the nucleins, *i. e.*, to the cell nuclei, have been mainly conducted by Kossel, Nencki and Sieber, Stadthagen,

[1] Folin, Zeit. f. physiol. Chem., xxiv, and Folin and Shaffer, ibid., 1901, xxxii. See also Rothlisberger, Schweiz. Woch. Chem. Pharm., 1905, Nos. 18 and 19.

Ebstein, and Horbaczewski. The chemistry of these compounds is mainly due to the most important researches of Emil Fischer. These authors have shown the clinical importance of these bases. According to our present knowledge, their formation depends upon the destruction of cellular elements, especially of the cell nuclei rich in nuclein. The following scheme may help the reader to understand the derivation of the purin bodies more clearly:



The purin compounds which occur in the urine are: Xanthin, guanin, hypoxanthin, adenin, heteroxanthin, paraxanthin, episarkin, epiguanin, methylxanthin, carnin. Heteroxanthin, paraxanthin, and methylxanthin are formed principally from the caffein, theobromin, and theophyllin of the food. The presence of guanin and carnin in the urine has not been made out with perfect certainty. The amounts of purin bases which are excreted in the twenty-four hours vary greatly. According to Emerson, 15.6 to 45.7 mg. are eliminated, while Camerer places the amount on a mixed diet at 87, on vegetable diet at 111, and on a meat diet at 44 mg. Concerning the pathologic significance of these compounds, but little is known, except that xanthin, hypoxanthin, and adenin are increased in leukemia, and that guanin is also found in this disease. Tuberculosis also appears to be associated with an increase in the purin bases. There also appears to be a certain antagonism between uric acid and the purin bases. When the latter are increased, the uric acid is excreted in lessened amount. Regarding the connection between the purin bases and the diazo-reaction, see p. 607.

Until lately, Kruger and Wulff's[1] method has been generally used to estimate the total amount of the purin bodies. But it has been proved inaccurate, and so will not be described.

Salkowski's method is exact. Is depends upon the precipitation of the purin bases by an ammoniacal silver solution. It determines the purin bases alone, and is analogous to the Ludwig-Salkowski method for estimating uric acid. Denigès' method is employed at the Bern Clinic quite successfully, and will also be described.

SALKOWSKI'S METHOD OF ESTIMATING THE PURIN BASES[2]

The precipitate obtained from the urine (at least 500 to 1000 cc.), by precipitating with the silver magnesia solution, is, after carefully washing, decomposed by hydrogen sulphid (just as in the Ludwig-Salkowski uric acid method, p. 638 et seq.). The filtrate is evaporated to dryness, and the residue extracted with 2 to 3 per cent. sulphuric acid. The latter dissolves the purin bases and leaves the uric acid undissolved. To be absolutely sure that at the most only traces of uric acid become dissolved, Salkowski delays filtering until the following day. The filtrate is now rendered alkaline with ammonia, and precipitated again with the silver solution. The amount of silver present in the precipitate is determined (after washing) by titration with ammonium thiocyanate. From the amount of silver present in the precipitate can be calculated the quantity of xanthin or purin bases present. One cc. of $\frac{1}{50}$ ammonium thiocyanate corresponds to 0.00152 gm. xanthin.

The amount of xanthin is either figured out or the xanthin bases are separated directly from the second silver precipitate and weighed.

[1] Zeit. f. physiol. Chemie, vol. xx, p. 176.

[2] Deut. med. Woch., 1897, No. 14, and Centralbl. f. d. med. Wiss., 1894, No. 30.

METHOD FOR THE DETERMINATION OF PURIN BODIES, INCLUDING URIC ACID, ACCORDING TO DENIGÈS[1]

This method is based on the fact that purin bases and uric acid are precipitated quantitatively by an ammoniacal solution of silver nitrate, ammonium chlorid, and magnesium chlorid, and that a permanent precipitate of silver iodid is produced by silver nitrate in an ammoniacal solution of potassium cyanid and potassium iodid only after all potassium cyanid has been changed to potassium silver cyanid. This test furnishes the quantity of purin bodies, including uric acid.

The following solutions are necessary:

1. A $\frac{N}{20}$ ammoniacal silver magnesium solution. In a measuring flask of 1 liter capacity are placed 150 gm. of pure ammonium chlorid and 100 gm. of pure magnesium chlorid; it is then filled three-quarters full with ammonium hydroxid. This is gently heated on the water-bath until the salts are dissolved. After cooling, 500 cc. of this fluid are mixed with 500 cc. of a $\frac{N}{10}$ solution of silver nitrate.

2. A $\frac{N}{10}$ solution of potassium cyanid. Ten gm. KCN are dissolved in about 1 liter of water, to which are added 10 cc. of ammonium hydroxid, and the whole is then filtered. This solution is too concentrated. It is so diluted with a $\frac{N}{10}$ solution of silver that 10 cc. of the latter correspond exactly to 20 cc. of the potassium cyanid solution, since 2 molecules of potassium cyanid react with 1 molecule of silver. (Formation of potassium silver cyanid, $KAg(CN)_2$). To standardize the potassium cyanid solution 20 cc. are placed in a beaker, and 100 cc. of water, 10 cc. of ammonia, and a few drops of potassium iodid solution are then added. Next, a sufficient quantity of the $\frac{N}{10}$ silver solution is added to produce a slight but persistent cloudiness. If we assume that for this purpose it is necessary to use $10 + n$ cc. of the silver solution, then there must be added to the potassium cyanid solution water in the proportion $2\ n$ cc. to each 20 cc. A potassium cyanid solution so prepared will correspond to an equal volume of the $\frac{N}{20}$ silver solution.

3. A solution of potassium iodid prepared by dissolving 20 cc. of potassium iodid in 100 cc. of water and adding 2 cc. of ammonium hydroxid.

4. A $\frac{N}{10}$ silver solution. Seventeen grams of pure and dry silver nitrate are dissolved in 1 liter of water.

These solutions are utilized in the following manner to determine the purin bodies of the urine. To 100 cc. of urine there are added 25 cc. of the ammoniacal $\frac{N}{20}$ silver magnesia solution. This is well shaken and the precipitate (consisting of silver combinations of the purin bases) filtered off. To 100 cc. of the filtrate, which correspond to 80 cc. of urine and 20 cc. of the silver solution, are added 20 cc. of the potassium cyanid solution. This volume of potassium cyanid solution would react exactly with 20 cc. of the silver solution if a part of the silver had not been used up by the purin bases, and thus been removed by filtration. Inasmuch as the quantity of silver is less, there will be an excess of potassium cyanid. This excess is estimated by adding as an indicator a few drops of potassium iodid solution, and then, from a buret, $\frac{N}{10}$ silver solution until a permanent cloudiness is produced. The amount of silver solution added will correspond exactly to the amount of silver held in combination by the purin bodies. By far the greater part of the purin precipitate is made up of uric acid, so that the final result, so far as uric acid is concerned, may be figured as follows:

Each cubic centimeter of the $\frac{N}{10}$ silver solution corresponds to 0.0168 gm. of uric acid. If n cc. silver solution have been used, these 80 cc. of urine will contain $n \times 0.0168$ and 1 liter of urine $\frac{0.0168 \times 1000 \times n}{80} = 0.21 \times n$ purin bodies in terms of uric acid.

QUANTITATIVE ESTIMATION OF OXALIC ACID

This estimation may have a certain amount of interest as indicating an abnormal breaking down of tissue. (See Oswald, p. 673.) The reader is referred to papers of Salkowski[2] and Autenrieth and Barth,[3] where quantitative methods are given.

[1] After C. Vieillard, L'urine humaine, Paris, 1898; original in Bull. de la soc. de pharm. de Bordeaux, 1884, p. 137.

[2] Zeit. f. physiol. Chemie, 1900, vol. xxix, p. 437. [3] Ibid., 1902, vol. xxxv, p. 327.

QUANTITATIVE ESTIMATION OF INDICAN

An approximate idea of the amount of indican in the urine may be had from the depth of color produced in the qualitative tests for this substance.

There are a number of methods which have been suggested for the quantitative estimation of indican, some of which are based on colorimetric principles, others which are based on titration. Most of these methods are too complicated for clinical purposes. One of the most convenient is that of Strauss.[1] The urine is oxidized with a reagent and the indigo formed is extracted with chloroform. The color of the chloroform is compared with a standard solution. Strauss uses for the extraction the separating funnel figured on p. 451. The funnel must be graduated in 5 cc. As a standard solution for comparison, Strauss employs a solution of 1 mg. of indigotin (Kahlbaum) in 1000 cc. of chloroform. Strauss' method is as follows: Twenty cc. of the urine are precipitated with 5 cc. of a 20 per cent. basic lead acetate solution. After filtering, 10 cc. of the filtrate are introduced into the separatory funnel and 10 cc. of Obermeyer's reagent (see p. 580) added. Five cc. of chloroform are now added, and the contents of the funnel shaken. It is then allowed to stand for two to three minutes. The liquid is extracted several times with chloroform until the reagent extracts no more of the indigo. The chloroform is then placed in a graduated cylinder, and diluted with pure chloroform until the color is equal to that of the standard solution of indigotin. With urines containing much indican the extraction must be repeated four or five times. The indigo solution must be placed in a test-tube of the same diameter as that of the indican solution. Both should be held in front of a white paper. If the total volume of the chloroform solution used for the extraction be 1 cc., and the amount of chloroform which was necessary to dilute the solution until it reached the tint of the comparison solution y, we obtain the volume x, to which the whole extract must be brought to give the requisite depth of color.

$$x = a\,\frac{y}{2}\ \left(\text{as } \frac{x}{a} = \frac{y}{2}\right).$$

This calculated volume of chloroform, to which the total chloroform extract must be brought is proportional to the amount of indigo extracted. Strauss found variations of the chloroform value from 5 to 10 cc. (normal) to 15 cc. in tuberculous peritonitis, chronic catarrh of the small intestines, and purulent peritonitis. More or less marked variations were found by the same observer in pulmonary tuberculosis, gastric carcinoma, pneumonia, acute rheumatic arthritis, acute endocarditis, typhoid, and acute perityphlitis.

As the standard indigotin solution contains 1 mg. in 1 liter, the amount of indican can be easily calculated. As the amount of urine used is only 8 cc. (10 cc. of urine + 5 cc. of basic lead acetate solution, and of this 10 cc. of the filtrate), the results must be calculated on this basis. Strauss estimates the amount of indican eliminated by a healthy person in terms of indigotin at 2 to 4 mg. in the twenty-four hours. With urines containing much indican, the amount may rise to 60 mg. and more. The method takes fifteen to twenty minutes.

The test solutions must be kept in the dark, and even then must be renewed from time to time. The author recommends that a more concentrated solution be prepared. This is more stable, and from this the requisite dilution may be made easily.

ESTIMATION OF THE KREATININ IN THE URINE

Kreatinin in the urine is probably derived from the kreatin of the muscles. Kreatinin is the anhydrid of kreatin. Normal urine probably does not contain kreatin. The excretion of kreatinin generally runs parallel to the excretion of urea. An increased ingestion of meat, and in all probability any augmentation of muscular metabolism, increases the excretion of kreatinin. Here lies the clinical interest in the quantity of kreatinin in the urine. The various results of experiment as to whether the kreatinin increases in amount with increased muscular work differ. It is generally assumed that the excretion of kreatinin is not increased by muscular exertion. According to Thomas and Späth,[2] the daily excretion of kreatinin of healthy men is about 1 gm. The excretion of kreatinin in disease

[1] Deut. med. Woch., 1902, No. 16, p. 299.

[2] Harnanalyse von Neubauer und Vogel, Neubearbeitet von Huppert und Thoma, Kriedel, Wiesbaden, 1890.

(in spite of its theoretic interest) has not been followed clinically very closely. A pronounced increase has as yet been noticed only during the fever of acute diseases.

Kreatinin behaves like uric acid in reducing cupric oxid and, therefore, interferes with Trommer's test for glucose. It does not reduce alkaline solutions of bismuth.

An accurate quantitative determination of kreatinin may be got (Neubauer) [1] by preparing and weighing the kreatinin zinc chlorid precipitated from the urine. Salkowski [2] has modified the Neubauer method. The original article must be consulted for the technic. (Compare Neubauer and Vogel[3]).

Kreatinin can be demonstrated qualitatively in the urine by either of the following two simple methods, which may also be used for a quantitative estimation:

Jaffe's Reaction.[4] The addition of a little aqueous solution of picric acid and a few drops of diluted sodium or potassium hydroxid to a solution of kreatinin will immediately produce an intense red color even when the amount of kreatinin in the urine is only 1 : 5000. The color will increase for a few moments, and then persist unchanged for hours. Acetone also gives a red color, although a much less intense one; hence, it is wise first to remove by boiling any acetone that may be present in the urine. Folin has used this reaction for the quantitative estimation of kreatinin (see Supplement).

Th. Weil's Reaction.[5]—A few drops of a very dilute solution of sodium nitroprussid are added to the urine, and then some diluted sodium hydroxid. If kreatinin is present, a ruby-red color will result, which soon changes to a yellow. Up to this point the reaction is identical with Legal's acetone test (p. 600 et seq.). If, however, acetone is present, the fluid turns red again when acidified with acetic acid; this is not the case with kreatinin. Salkowski claims that if kreatinin is present, the addition of acetic acid and subsequent heating produce a greenish and then bluish coloration (Prussian blue). Before attempting Weil's test, the acetone may be expelled by boiling the urine.

THE QUANTITATIVE ESTIMATION OF KREATININ AND KREATIN IN THE URINE, ACCORDING TO THE METHOD OF FOLIN AND GOTTLIEB.

The researches of Gottlieb and of Stangassinger[6] have shown that kreatin and kreatinin play an important rôle in the general metabolism, and not, as was formerly assumed, only in the metabolism of muscles; accordingly, it is quite possible that the estimation of these bodies in the urine will in the future become of some clinical importance. We shall, therefore, briefly notice the methods of estimating the bodies in the urine. The older method, proposed by Neubauer and Salkowski, is quite complicated, and Gottlieb and Stangassinger have, therefore, made use of a modified procedure introduced by Folin.

The Estimation of Kreatinin.—Folin's method of estimating kreatinin depends upon a modification of Jaffé's reaction for this body, which enables quantitative results to be obtained. (See Reduction of Kreatinin to Picramic Acid with the Production of Red Color by the Use of Picric Acid in an Alkaline Solution.) Folin makes use of a Dubosq colorimeter with two tubes. One tube is filled with a standard fluid consisting of a normal solution of potassium dichromate, while the other is filled with urine in which red coloration has been produced by the method of Jaffé. The instrument is so constructed as to enable one to set the level of fluids within 1 to 10 mm., and to read off these levels on a scale when, by transmitted light, the color of the fluids in the tubes

[1] Ann. d. Chemie. u. Pharm., 1861, vol. cxix, p. 33. Modification der Methode durch Salkowski, Zeit. f. physiol. Chemie, 1886, vol. x, p. 113.
[2] Zeit. f. physiol. Chemie, 1886, x, 113.
[3] Die chem. u. mikroskopische Untersuchung des Harnes, 1903.
[4] Zeit. f. physiol. Chemie, 1886, vol. x, p. 399.
[5] Th. Weil, Ber. d. chem. Gesellschaft, vol. xi, p. 2175.
[6] Zeit. f. physiol. Chemie, Bd. lii, and lv.

approaches the other most closely. From these figures the kreatinin content may be calculated by the use of colorimetric principles, if the color value of the standard fluid used for comparison has been estimated. For making the estimation one tube is filled with standard fluid up to the mark 8 mm. Then 10 to 20 cc. of urine (the exact quantity needed is determined by repeating the test) are placed in a flask with a mark at 500 cc., and to these are added 15 cc. of a 12 per cent. solution of picric acid and 5 cc. of 10 per cent. solution of sodium hydroxid. After ten minutes the color reaction assumes its maximum; then the mixture is diluted with water until the total volume equals 500 cc., and a portion of it is placed in the second tube of the colorimeter, which is then adjusted so that the colors of the fluids in the tubes approximate each other. The color of the standard fluid corresponds to 0.01 kreatinin in 500 cc., and the amount in the urine tested can, therefore, be easily estimated from the figures obtained. Gottlieb and Stangassinger have retained the principle of Folin's method, but have constructed a simpler and a cheaper colorimeter which is manufactured by Runne in Heidelberg; in this instrument the prisms of the original colorimeter are replaced by plane mirrors. A cut of the apparatus appears in the paper in Vol. lii of the Zeit. f. physiol. Chemie, quoted above. From their researches they concluded that this method of estimating kreatinin by comparing with a standard solution of dichromate of potassium gives exact results when the level of the kreatinin solutions ranges from 4.2 to 14 mm.; they, therefore, always attempt to bring the levels of the fluid between these ranges before the reading is made, if there is sufficient material for the purpose. If the material on hand allows of one estimation only and the approximate kreatinin content of it is unknown, they make use of a table constructed experimentally by measuring standard kreatinin solutions in the apparatus. This table gives the amounts of the solution of kreatinin containing 1.5, 14, and 20 mg. in 500 cc. that would correspond in color to that of 8 mm. of the standard solution of the dichromate in the colorimeter. Any intervening values may be easily interpolated in this table. According to Dreibholz,[1] the presence of sugar in the urine does not interfere with the accuracy of the test.

The Estimation of Kreatin.—The statement made on p. 643 of this book that normal urine contains kreatinin, but probably no kreatin, must be corrected, because of the results obtained by Folin and Klercker since the statement has been made. They have shown that kreatin does appear in the normal urine, and it is, therefore, possible that estimation of this body in the urine may likewise assume some importance in the future. The attempt has been made to apply Folin's method to the estimation of kreatin.

[**The Nitrogen Partition.**—Recently in America and England a more detailed scheme of analysis of the urine has been employed for the purposes of diagnosis. It has been used to determine whether the organs concerned in the elaboration of the end-products of metabolism are at fault.

Such a scheme of analysis involves the determination of total nitrogen, ammonia nitrogen, urea nitrogen, kreatin and kreatinin nitrogen, and uric acid nitrogen. These latter amounts are added together and

[1] Dreibholz, Zur Frage der Kreatininausscheidung im Harn, Inaugural Dissertation, Greifswald, 1908.

the sum subtracted from the total nitrogen. This gives a remainder, which is called the undetermined or rest nitrogen.

Some investigators have devoted their attention to the ammonia nitrogen alone, others have examined closely the kreatinin nitrogen or the undetermined nitrogen, while some have viewed the complete analysis as a whole in an attempt to use the results for the purposes of diagnosis. The conditions to which this form of analysis has been more particularly applied are the toxic states of pregnancy, typhoid fever, and pneumonia.

The way in which the analyses have been employed is to take urines of normal individuals which have been examined by this method and use them as standards for comparison.

The difficulties in the interpretation of this class of analyses are very great. One chief difficulty lies in the fact that the number of normal cases examined has not been sufficient to establish the limits between which a normal urine may vary. A second is that in most instances patients suffering from typhoid fever or vomiting of pregnancy are in a state of undernutrition. They are either receiving no food, or the amount is quite insufficient for the needs of the body. This state of undernutrition has by itself, and quite independently of any actual pathologic condition, a profound effect on the composition of the urine. The amount of information which is at present available concerning the distribution of the nitrogen in cases of undernutrition in normal individuals is very scanty, so that a complete and satisfactory set of standards with which to compare pathologic cases is wanting.

While the method of diagnosing a pathologic condition from a consideration of the nitrogen partition suffers at the present moment from lack of data, it is believed future work in this field will demonstrate that it may perform a useful function. Its value is at present under discussion.[1]—C. G. L. W.]

QUANTITATIVE ESTIMATION OF THE CHLORIDS IN THE URINE

The amount of chlorids eliminated in the urine of a healthy adult in twenty-four hours varies between 11 and 15 gm., calculated as sodium chlorid. Chlorids of the urine are diminished in hunger and diarrhea, from the formation of exudates or transudates rich in sodium chlorid, and in fever.

It has been assumed that the diminution of chlorids eliminated in the urine in fever depends entirely upon the diminished ingestion of food. This is certainly wrong, because in some other cases, when much less food is ingested, no such marked diminution of the chlorids appears in the urine, as, for example, in pneumonia. Again, in pneumonia the amount of chlorin eliminated increases very markedly immediately after the crisis without any increased ingestion of food. No absolutely correct explanation of the diminution of chlorin in fever has yet been advanced. One theory suggests that in fever the cell-proteins, which are relatively poor in chlorin, are disintegrated much more extensively than the circulating proteins. Another theory is that the formation of inflammatory exudates deprives the urine of a considerable amount of chlorin. This

[1] Recent discussion of the value of the nitrogen partition will be found in Ewing and Wolf, Amer. Jour. Med. Sci., 1906, cxxxi, 751; Amer. Jour. Obstet., 1907, lv, 289; Arch. Int. Med., 1909, iv, 330; Underhill and Rand, ibid., 1910, v, 61.

agrees very well with the fact that in no other disease is there so great a diminution in the amount of chlorin as in croupous pneumonia, where exudation is very acute. The author has found a decrease of chlorids in the blood, which is in accordance with this view. A third assumption is that the chlorids are kept back as a sequence of the supposed retention of water in fever. Probably several of the above-mentioned factors act together in febrile disturbances to diminish the chlorids in the urine. In pneumonia the retention of chlorids in the exudate is probably the most important factor.

It is practically important, however, to remember that in febrile diseases any improvement in the condition will increase the amount of chlorids in the urine, and often before any improvement is indicated by the thermometer—*e. g.*, in pneumonia. Any great diminution in the amount of chlorids in non-febrile disorders always points to a serious condition. On the other hand, there are some very severe general conditions (the author has paid particular attention to this in circulatory disorders) in which no diminution of chlorids is observed.

A pronounced diminution or absence of chlorids in the urine in a febrile disorder will always suggest pneumonia, because, as has already been mentioned, the greatest degree of diminution is reached in this disease.

According to Emerson, the chlorin elimination may be used for the differential diagnosis between meningitis, when the chlorids are markedly decreased, and typhoid, when only a relatively small decrease takes place. Marked decreases have been observed by Emerson in pyemia, puerperal fever, cholera, and acute rheumatic arthritis. An increase was observed in cirrhosis of the liver. In nephritis, according to Achard and Löper, the excretion of chlorids is lower the more acute the condition. The excretion is the least disturbed in contracted kidney.

For practical purposes an approximate estimation of the chlorids, made as follows, will suffice: A specimen of urine in a test-tube is acidified with about 10 drops of pure nitric acid. Then a single drop of silver nitrate solution (1 : 10) is added. If the chlorids are normal, a solid ring, a ball, or one or more compact lumps of silver chlorid form and settle to the bottom; if diminished, only a more or less intense cloudiness arises. With a little practice the relative amount of chlorids may be judged by this simple test. Nitric acid is employed because it precipitates any protein present, which otherwise would be precipitated by the silver solution, and might thus lead to deception; and also because it prevents the precipitation of silver phosphate, which might be mistaken for the silver chlorid. If a large amount of protein appears after the addition of the nitric acid, it must first be removed by filtering or by letting it settle to the bottom before performing the chlorid test.

Volhard's procedure (titration with silver and ammonium sulphocyanate solution) is the most reliable method. It is described in connection with the Lütke-Martius method of estimating the hydrochloric acid of the gastric juice, and can also be employed for the urine. (See p. 455 et seq.) In employing this method it is best to use the urinary ash, since, if the silver solution is added to the urine, it precipitates not only the chlorids, but also the purin bodies, which would consequently give rise to a slight error.

QUANTITATIVE ESTIMATION OF THE PHOSPHATES IN THE URINE

The daily excretion of phosphoric acid in the urine, in the form of phosphates, amounts normally to 2 to 3 gm. The ratio of the excreted phosphoric acid to the amount of excreted nitrogen is normally 0.18 (15 urea = 7 nitrogen). This ratio, $\frac{P_2O_5}{N}$, is termed the relative value of the phosphoric acid excreted. In febrile conditions the absolute value of phosphoric acid elimination may be diminished or increased (more frequently the first), but Zülzer claims that the relative value is constantly diminished. In convalescence the absolute and relative values immediately increase to normal or sometimes above. According to Fleischer, a considerable diminution in the absolute, as well as the relative, phosphoric acid values seems to be constant in nephritis.

According to Emerson,[1] 60 per cent. of the phosphoric acid is normally excreted in the form of diacid, 40 per cent. in the form of monoacid, salts. An amphoteric reaction in the urine is found when the diacid phosphates are 30 to 50 per cent., and the monoacid 70 to 50 per cent., of the total phosphoric acid excretion. The phosphates of calcium and magnesium are relatively to the alkaline phosphates as 1 : 2 (Emerson). According to Gourod, the estimation of the earthy phosphates may be used for the differential diagnosis of pneumonia and tuberculosis. In the former they are diminished, in the latter, increased.

APPROXIMATE ESTIMATION OF PHOSPHATES WITH BOURGET'S PHOSPHATOMETER

An approximate idea of the total phosphoric acid may be made by measuring the amount of precipitate formed in a certain volume of urine with magnesia mixture. The earthy phosphates may likewise be estimated by using ammonia. Bourget has constructed an instrument[2] for this purpose which has found considerable favor in France. It consists of a tube 35 cm. high, the upper third of which has a diameter of 3 cm. The lower two-thirds have an internal diameter of 5 to 6 mm. Over the lower end of the tube a piece of muslin is placed carrying a disk of filter-paper, the muslin and paper being fastened to the tube by a piece of rubber tubing, which projects below the end of the tube. The end of the rubber tube is closed with a rubber stopper. There are two marks on the upper wide part of the tube, one for reagent and one for urine. The lower portion of the tube carries an empirical scale, giving directly the percentage of phosphoric acid in the urine.

To estimate the total phosphoric acid an ammoniomagnesia mixture of the following composition is used:

Magnesium sulphate	30.00
Ammonium chlorid	30.00
Ammonia	130.00
Water	130.00

The phosphatometer is filled with this solution to the mark R, and then urine, previously acidified with 2 or 3 drops of hydrochloric acid, is added to the mark U. The two are mixed and the whole apparatus filled with dilute ammonia, 1 to 3. The stopper closing the end of the rubber tube is then removed, and the instrument fixed by means of a loosely fitting cork in the mouth of a flask. The liquid filters gradually and the precipitate collects in the lower end of the tube. It consists principally of ammoniomagnesium phosphate. As soon as the liquid is completely filtered off, the upper level is read on the scale, and the amount is given directly in tenths of a per cent.—1 cm. of precipitate corresponds to 0.14 per cent. PO.

The approximate estimation of the earthy phosphates must be preceded by the estimation of the total phosphates. Twenty-five cc. of the urine are measured off, 15 to 20 drops of ammonia added, and allowed to stand until the earthy phosphates are precipitated. The urine is then filtered into the phosphatometer, and a total phosphate estimation made. The difference between the two readings gives the amount of earthy phosphates in the urine.

The quantitative estimation of phosphates is accomplished by titration with uranium nitrate in a solution of acetic acid, which precipitates all the phosphates. The end-reaction is either the brown color which is produced by an excess of

[1] Clinical Diagnosis, Philadelphia, 1906.

[2] Bourget, Manuel de chimie clinique, Paris, 1901. The phosphatometer may be obtained from Penfoldt, Rue de l'université, Geneva.

uranium nitrate in the presence of potassium ferrocyanid, or the green color formed by tincture of cochineal with a surplus of uranium.

The following solutions are required:

1. A solution of uranium nitrate, which must be standardized with a solution of disodium phosphate of known strength. About 35 gm. of uranium nitrate are dissolved in a liter of water.

2. A solution of disodium phosphate, so prepared that 50 cc. shall contain 0.1 gm. P_2O_5. This solution is prepared from the ordinary pure disodium phosphate; but since this salt contains a varying quantity of water, and consequently a varying amount of P_2O_5, the solution must be standardized. This is done as follows: Twelve gm. of pure disodic phosphate are dissolved in a liter of water, and 40 cc. of the solution are titrated with $\frac{N}{10}$ hydrochloric or sulphuric acid, alizarin red being employed as an indicator. The end-reaction corresponds to the moment when all the disodium phosphate is transformed into the monosodium phosphate, and is indicated by the red solution turning yellow. If the solution is correct—*i. e.*, if 50 cc. contain 0.1 P_2O_5—the 40 cc. should require 11.25 cc. $\frac{N}{10}$ hydrochloric acid before the end-reaction occurs. As a rule, more is required, and the original solution must consequently be diluted. For example, if 13 cc. $\frac{N}{10}$ hydrochloric acid are required, and x represents the amount of fluid to which the 40 cc. must be diluted, we have the proportion:

$$40 : 11.25 = x : 13$$

$$\text{and } x = \frac{40 \times 13}{11.25}$$

The sodium phosphate solution must then be so diluted that every 40 cc. is brought up to the volume x. If the solution contains too little phosphate, it must be concentrated by evaporation according to a corresponding proportion.

3. Acetic acid sodium acetate solution: One hundred gm. of sodium acetate are dissolved in 800 gm. of water, 100 cc. of a 30 per cent. acetic acid solution are added, and the mixture is diluted to 1 liter.

4. Potassium ferrocyanid solution: 10 : 100 water or tincture of cochineal. The latter is prepared by dissolving 6 gm. of powdered good cochineal in a mixture of 300 cc. of distilled water and 200 cc. of alcohol. The mixture is kept at an ordinary temperature for several hours, during which time it is frequently shaken and is then filtered.

Preparation of the Uranium Nitrate Solution.—Fifty cc. of the prepared solution of sodium phosphate are placed in an Erlenmeyer flask, treated with 5 cc. of the acetic acid sodium acetate solution, and heated to the boiling-point. A solution of uranium nitrate (35 : 1000) is now added from a buret as long as there is a distinct precipitate formed. The solution should now be tested after the addition of every ½ cc. by taking a drop of the fluid out of the flask by means of a glass rod, and mixing it upon a porcelain plate or on a special paper prepared for the purpose by Schleicher and Schüll, with a drop of a potassium ferrocyanid solution. The end-reaction is the appearance of a reddish-brown color. A simpler method of attaining the same end is to add several drops of the tincture of cochineal to the fluid in the flask, bring it to the boiling-point, and add the uranium nitrate solution until a permanent pale-green color is obtained after mixing and reheating. It is now known how much uranium nitrate solution is necessary for the precipitation of 50 cc. of the sodium phosphate solution, and the uranium solution is to be diluted so that exactly 20 cc. will precipitate 50 cc. of the sodium phosphate solution. The 20 cc. of uranium solution are then equivalent to 0.1 P_2O_5 or 1 cc. is equivalent to 0.005 gm. P_2O_5. This varies somewhat according to the amount of uranium solution which is used. For this reason the standardization is performed with phosphate solution which corresponds fairly closely to the phosphoric acid content of normal urine. Using 20 cc., the amount is, according to Emerson, 4.98 mg.; for 21 cc., 5 mg.; for 40 cc., 5.14 mg.

Estimation of the Total Phosphates in the Urine.—If proteins be present, they must be removed; sugar does not interfere with the reaction. We proceed with the urine exactly as we did in the preparation of the uranium nitrate solution—*i. e.*, we titrate 50 cc. of the urine and 5 cc. of the acetic-acid sodium acetate solution at the boiling-point with the standardized uranium solution until the end-reaction is obtained with potassium ferrocyanid or cochineal. Every cubic centimeter of the uranium solution employed then corresponds to 0.005 P_2O_5.

Separate Estimation of the Earthy Phosphates.—In reference to so-called phosphaturia (see pp. 648 and 676), it is of interest to make a separate estimation of the earthy phosphates. The difference between the total phosphoric acid and the earthy phosphates then gives the alkaline phosphates. To estimate the earthy phosphates we proceed as follows: 100 cc. of urine are rendered alkaline with ammonia; the mixture is allowed to stand for twelve hours; the precipitate removed by filtration, and washed with ammonia water. The filter is now perforated with a glass rod, and the precipitate is washed into a beaker. After dissolving the precipitate by heat in as small a quantity of acetic acid as possible, the solution is diluted to 50 cc. with water, 5 cc. of the acetic acid sodium acetate solution are added, and the mixture is titrated with the uranium solution, as in the estimation of the total phosphates.

QUANTITATIVE ESTIMATION OF SULPHURIC ACID AND OF THE COMBINED SULPHURIC ACID

Although the total amount of sulphuric acid eliminated is as yet of no particular clinical importance,[1] the amount of the combined sulphuric acid—*i. e.*, sulphuric acid united with organic substances—*e. g.*, phenol, indol, etc.—to form the so-called ethereal sulphates is of much greater interest.

We can estimate sulphuric acid proper separately from combined sulphuric acid by titration, because in a urine which either is not acidified or is acidified entirely by acetic acid, barium solutions will precipitate only the sulphuric acid proper as barium sulphate; whereas in the presence of hydrochloric acid the ethereal sulphuric acid will be freed from its combinations and will be precipitated along with the inorganic sulphuric acid. By subtracting the value of the sulphuric acid proper from that of the total sulphuric acid, the amount of combined sulphuric acid may be obtained.

A process giving an approximate idea of the amount of sulphur has been suggested by Emerson.

In a large test-tube holding 25 cc. 3 volumes of urine are mixed with 1 volume of an acid barium chlorid solution containing 4 parts of barium chlorid, 1 part of hydrochloric acid, and 16 parts of water. The sulphates are precipitated as barium sulphate. If a milky opalescence takes place, the sulphates may be considered normal. If the precipitate is denser, the sulphates are increased. With a faint opalescence the sulphates are diminished. With a normal amount of sulphates, the precipitate occupies about half the concave portion of the test-tube. If the precipitate be filtered off, and hydrochloric acid added to the filtrate and the whole boiled, a further precipitate takes place, due to the ethereal sulphates.

FOLIN'S METHODS FOR TOTAL SULPHUR, TOTAL SULPHATES, ETHEREAL SULPHUR, AND NEUTRAL SULPHUR

Total Sulphur.—Place 25 cc. of the urine in a nickel crucible holding 250 to 300 cc., and add 3 gm. of sodium peroxid. Evaporate the mixture to a syrup on a water-bath, and heat carefully over a flame until it solidifies. Remove the crucible from the flame and allow it to cool. Moisten the residue with 2 cc. of water. Add 7 to 8 gm. of sodium peroxid to the residue, and fuse the mass over a flame. The fusion must be done carefully at first as the melt has a tendency to foam. Allow the crucible to cool thoroughly, and add 100 cc. of water. Allow the crucible to stand on the water-bath for some time, to dissolve the melt. Rinse the contents of the crucible into a flask and dilute to 250 cc. Add, slowly, 20 to 30 cc. of hydrochloric acid, and boil for thirty minutes. The solution should become almost clear. To the clear solution add 5 cc. of dilute alcohol (1 to 4), and boil again for five minutes. The addition of a few drops of methyl-orange solution will indicate whether any free

[1] The so-called total sulphuric acid of the urine consists of sulphuric acid in the ordinary sense of the word, and of sulphuric acid in combination—*i. e.*, with various organic substances.

chloric acids are present in the solution. In their absence the solution will not be decolorized. If the boiling has been sufficiently prolonged, this will be the case. The solution is now filtered, allowed to cool, and to it are added, by means of a test-tube or a thistle-tube drawn out to a fine point, 10 cc. of 10 per cent. barium chlorid solution. The addition of the 10 cc. should occupy about three minutes. During this time the solution is not stirred. The beaker is allowed to stand for two days, and filtered off on a Gooch crucible, ignited, and weighed. If Gooch crucibles are not available, the precipitate may be filtered through a Schleicher and Schüll ashless filter-paper, washed with cold water, ignited, and weighed.

Total Sulphates.—Place 25 cc. of the urine in a 200 to 250 cc. flask, add 20 cc. of dilute hydrochloric acid (1 to 4), and boil the mixture gently for twenty to thirty minutes. The mouth of the flask should be covered with a watch-glass. Cool and dilute to 150 cc. with water. Add 10 cc. of a 5 per cent. solution of barium chlorid, as in the total sulphur estimation. Allow the mixture to stand for at least one hour, and filter through a Gooch filter. Ignite and weigh.

Inorganic Sulphates.—Place 50 cc. of urine and 100 cc. of water in a 200 cc. flask. Add 10 cc. of dilute hydrochloric acid (1 to 4), without boiling, add 10 cc. of 5 per cent. barium chlorid solution drop by drop, and proceed as in the determination of total sulphates.

Ethereal Sulphates.—The difference obtained between the results obtained for total sulphates and for inorganic sulphates gives the amount of ethereal sulphates present in the urine.

The normal daily excretion of total sulphates in the adult amounts to 1.5 to 3 gm. of SO_3, and parallels the quantity of protein decomposed. The normal ratio of the daily amount of the total sulphates to the daily quantity of urea is about 1 : 5, while the ratio of the quantity of the ethereal sulphates to that of the remaining sulphates is about 1 : 10.

It is of some diagnostic interest that in many putrefactive processes phenol-like substances are formed in the urine, and at this time the ethereal sulphates are increased. Experiments which have been made to determine to what extent this may be used as an index of intestinal putrefaction have not been conclusive. Neither the relation of the ethereal sulphates to the total sulphates nor the absolute amount of the excretion give any decided information. The reason for this is that the ethereal sulphates are not altogether dependent on putrefactive processes, for other factors, such as the food and the breaking down of tissue, yield these substances in the urine. (See Jaffé, Indicanurie, Deutsche Klinik, 1907, vol. xi, p. 203.)

QUANTITATIVE ESTIMATION OF AMMONIA IN URINE

The normal amount of ammonia contained in adult urine, according to Neubauer, varies in twenty-four hours between 0.3 and 1.2 gm., and averages 0.7 gm. A meat diet, the ingestion of radishes, the breathing of air saturated with tobacco smoke, and the taking of ammonium salts and mineral acids as medicaments increase the daily amount of ammonia excreted.

The quantitative estimation of ammonia in the urine may be of clinical interest under certain circumstances. We know that the human organism, like that of carnivora in general, reacts to an increased ingestion of acid or increased acid formation by an increased production of ammonia, which serves the purpose of holding the otherwise injurious acids in combination. Consequently, the amount of ammonia salts contained in urine is an important indicator of acid metabolism.

The daily quantity of ammonia excreted is increased pathologically in diseases of the liver and in acute febrile diseases, such as pneumonia and typhoid fever. The increase is usually at the expense of the urea. In affections of the liver there is a specific impairment of its urea-forming function; in febrile diseases the increased quantity of ammonia is the effect of the increased formation of acids in consequence of the augmented decomposition of protein. The increase in the amount of excreted ammonia is most striking in diabetic acidosis.

This is of practical importance in diabetes mellitus. The increased elimination of ammonia led in this case to the discovery that certain diabetic urines con-

tain β-oxybutyric acid (compare p. 653), and that the amount of ammonia eliminated indicates in an approximate manner the degree of acidosis.[1]

To be sure, the amount of ammonia in the urine is not exactly parallel to the acid formation in the organism, because the ammonia becomes serviceable for the neutralization of acids only when the available fixed alkalis are no longer sufficient.

Magnus-Levy makes the following estimation: About 1 to 2 gm. of the ammonia excreted by a diabetic are for the purpose of neutralizing the fixed excess of acid resulting from the protein diet, and only the remainder is the measure for the pathologic excretion of acid. A diabetic with 4 gm. of ammonia in the urine is consequently excreting not twice, but nearly three times, as much pathologic acid as one with 2 gm., since 1 gm. or more of the 2 or 4 respectively is combined with the acids normally excreted. According to this supposition, when 2 gm. of ammonia are excreted, about 1 gm. is utilized for combination with the two pathologic acids of diabetes (oxybutyric and aceto-acetic acid); while an elimination of 5 gm. leaves 3 to 4 gm. for this purpose. An excretion of 8 gm., which is but rarely observed, gives 6 to 7 gm. of ammonia as the measure of the pathologic amount of acids. These figures correspond to 6, 20, and 36 to 40 gm. of β-oxybutyric acid. Magnus-Levy also points out that such an estimation of the acids from the ammonia is of value only when an average is taken from the observations extending over several days, since the amount of ammonia formed in any twenty-four hours will vary considerably as the result of the temporary retention or excretion of alkalis. The large quantity last mentioned, of 40 gm. of β-oxybutyric acid, he says, represents the maximum quantity of acid which the body can neutralize by producing ammonia and without the administration of sodium bicarbonate. By administering 40 gm. of this substance, however, the organism may eliminate 60 gm. of β-oxybutyric acid daily in the urine. Magnus-Levy believes that this latter quantity is exceeded only in diabetic coma.

SCHLÖSING'S METHOD FOR THE ESTIMATION OF AMMONIA

Schlösing has described the simplest method for estimating the amount of ammonia. It depends upon the fact that aqueous solutions of ammonia readily part with their ammonia when exposed to the air, and that when dilute sulphuric acid is placed in a closed chamber near the ammonia, the acid quickly and completely absorbs the ammonia. Therefore, if we free the ammonia from a known quantity of urine by the addition of lime-water, and then allow it to become absorbed in a closed space by a known amount of sulphuric acid, the amount of absorbed ammonia can easily be determined by a simple acidity titration. Neubauer proceeds as follows: A shallow dish with vertical sides containing 25 cc. of filtered urine is placed upon an exsiccator plate. A triangular glass is set over the top of the dish and holds another vessel containing 10 cc. of normal sulphuric acid. At least 10 cc. of lime-water are now added to the urine, and the whole is then quickly covered with the glass bell of the exsiccator, whose margin is greased with tallow. All the ammonia in the urine will be absorbed by the acid within three or four days. Then, using methyl-orange as an indicator, the acid is all titrated with $\frac{N}{4}$ sodium hydroxid until the red color turns to yellow. Every cubic centimeter less than 40 of the sodium solution employed corresponds to $\frac{17}{4}$ mg. of NH_3.

The objection to Schlösing's method is the length of time required for the estimation.

Schmiedeberg's[2] platinum chlorid method may be more quickly carried out than Schlösing's, but it is also more complicated.

METHOD FOR AMMONIA ESTIMATION OF KRÜGER AND REICH

This method is based on the first observations of Boussingault, and has since been modified by Shaffer, the above-mentioned authors, and Schittenhelm. The method depends on the fact that ammonia distils off at a low temperature when the pressure is low, from solutions containing it when they are made alkaline.

Twenty-five cc. of the urine to be examined are placed in a distilling flask holding 500 cc.; 10 gm. of sodium chlorid and 50 cc. of methyl-alcohol are added. The side neck of the flask is connected with two gas washing-bottles containing a known

[1] *Cf.* Naunyn, Diabetes Mellitus, in Nothnagel's Sammelwerke, 1898, p. 179; and Magnus-Levy, Arch. f. exp. Path., 1899, vol. xlii, p. 1981.

[2] Arch. f. exp. Path., vol. vii, p. 166.

volume of standard sulphuric acid. The distilling flask is heated on the sulphuric acid. The distilling flask is heated on the water-bath at 60° C. At this temperature all the ammonia is distilled off and collected in the acid. The acid remaining unneutralized is determined with standard alkali. From this the amount of ammonia distilled off is calculated.

METHOD FOR AMMONIA ACCORDING TO FOLIN

Place 25 cc. of urine in an areometer cylinder about 30 to 40 cm. high. Add about 1 gm. of dry sodium carbonate and a little kerosene oil to prevent foaming. Insert into the neck of the cylinder a rubber stopper provided with two perforations, into each one of which passes a tube, one of which reaches below the surface of the liquid. The shorter tube (10 cm. in length) is connected with a calcium chlorid tube filled with cotton-wool, and this tube is connected with a gas washing-bottle containing 20 cc. of decinormal sulphuric acid and 100 cc. of distilled water. A few drops of an indicator, either alizarin red or carminic acid, are added. To complete the absorption of the ammonia the gas washing-bottle is provided with a special tube which insures better contact of the air which passes through it with the acid. The other tube of the gas washing-bottle is connected with a good filter-pump, and air drawn through the apparatus for an hour and a half. The number of cubic centimeters of acid neutralized by the ammonia may be determined by direct titration with decinormal sodium hydroxid. This is one of the most satisfactory methods for the determination of ammonia which has yet been devised. Several determinations may be made simultaneously by connecting the set of apparatus in tandem.

QUANTITATIVE ESTIMATION OF THE β-OXYBUTYRIC ACID IN THE URINE

The quantitative estimation of β-oxybutyric acid is of great interest in diabetic acidosis. Stäubli [1] has shown that in benign cases of acidosis, in spite of a high content of acetone and aceto-acetic acid, the amount of oxybutyric acid in the urine is small. If this be the case, the estimation of this acid in the urine is a matter of considerable prognostic importance. The estimation of the acid by means of the polariscope is a practical clinical method. β-oxybutyric acid is levogyrate, and has a specific rotating power of 24.1, or of 20.6°, according to different authorities. Fermented urine is freed from protein and decolorized with lead acetate and ammonia or mercuric nitrate, and its rotatory power is then determined (p. 624 et seq.). If the 100 mm. tube of the polaristrobometer is used (p. 625), Minkowski states that a rotation of −1° will correspond to $\frac{100}{20.6}$ per cent. of β-oxybutyric acid (about 5 per cent.). In this estimation we must naturally assume that the urine does not contain any other non-fermentable substances which are levogyrate, such as the combined glycuronates, etc. A positive Trommer's test with the fermented urine would point to their presence. The normal constituents of the urine which turn the plane of polarized light to the left, such as uric acid and kreatinin, do not disturb the test, because the rotation caused by them is very slight, and, besides, there is only a very small percentage of them in diabetic polyuria.

Magnus-Levy [2] regards the quantities obtained by this method as inaccurate, and thinks they are too large, but is unable to give a satisfactory explanation of the marked levogyration found in these cases.

Bergell [3] (see Stäubli [4]) estimates β-oxybutyric acid by making 200 cc. of the urine alkaline with sodium carbonate and evaporating to a syrup. The urine is then made acid with phosphoric acid, and mixed with kieselguhr until it forms a dry powder. This is then extracted with ether in a Soxhlet apparatus for thirty-six hours. The ether residue is diluted to 20 cc., decolorized with animal charcoal, or with lead carbonate and hydrogen sulphid, and the acid estimated polarimetrically.

For clinical purposes the quantitative estimation of the excretion of ammonia is the best indirect means for determining the amount of β-oxybutyric acid excreted.

Darmstädter's [5] method for the direct estimation of the β-oxybutyric acid

[1] Korrespondenzbl. f. Schweiz. Aerzte, 1908, No. 5.
[2] Arch. f. exp. Path., vol. xlii, p. 167, et seq.
[3] Zeit. f. physiol. Chemie, xxxiii, 310.
[4] Korrespondenzbl. f. Schweiz. Aerzte, 1908, No. 5.
[5] Zeit. f. physiol. Chemie, 1902–03, vol. xxxvii, p. 355.

depends upon the fact that β-oxybutyric acid is broken up into crotonic acid and water by concentrated mineral acids. The method is carried out as follows: 100 cc. of urine are rendered alkaline with sodium carbonate and evaporated almost to dryness; the residue is dissolved in 150 to 200 cc. of 50 to 55 per cent. sulphuric acid; 300 to 350 cc. are now distilled from this mixture within two to two and one-half hours, the fluid removed being replaced by water; the distillate is now shaken two or three times with ether, the ether evaporated, and the residue heated to 160° C. in order to remove any volatile fatty acids which may be present. The residue is then dissolved in 50 cc. of water, the solution filtered, and titrated with $\frac{N}{10}$ sodium hydroxid solution: 1 cc. $\frac{N}{10}$ sodium hydroxid solution equals 0.0086 crotonic acid; 1 part crotonic acid equals 1.21 β-oxybutyric acid.

Magnus-Levy did not find that in this process the β-oxybutyric acid was completely converted into crotonic acid.

Magnus-Levy [1] extracts the urine directly. To every 100 cc. of the fresh urine 30 to 40 gm. of ammonium sulphate are added, and 15 to 20 cc. of 20 per cent. sulphuric acid. For large amounts of urine the extraction apparatus of A. Czelmannowitz is used, which allows one to operate on 300 to 1500 cc. of urine at one time. For smaller amounts one of the ordinary liquid extraction apparatus may be used. No fixed time for extraction can be given. In any event the completeness of the extraction must be controlled. According to the rapidity with which the ether percolates through the urine the process takes twenty-four to seventy-two hours. After twenty-four hours,[2] the ether is removed from the extraction flask, filtered through a dry filter, and allowed to evaporate spontaneously in a porcelain dish. It is better not to heat the residue on the water-bath. The residue is a syrup containing crystals of hippuric acid. To the residue are added 8 to 16 cc. of water. An oil falls to the bottom which later becomes crystalline. The liquid is filtered through a small filter and made up to 10 to 20 cc. A small amount of kieselguhr may be added to clarify the liquid, which must then be filtered through a dense filter-paper. The liquid is then polarized. If the second and third extractions do not show any residue, the extraction may be stopped. The watery solutions of the ethereal extraction are perfectly clear, and are so little tinged that they may be polarized at once in a 20 cm. tube. As the rotatory power of the acid is great, one may estimate small amounts of the acid with considerable accuracy. If 1500 cc. of urine be passed containing 0.6 gm. of the acid, and of this 1000 cc. be used for the estimation, 0.4 gm. in 10 cc. of water will give a rotation of $-1.8°$ in a 20 cm. tube. With urines containing more of the acid one must use correspondingly smaller amounts for the process. Magnus-Levy gives the specific rotation of oxybutyric acid as 24.12°.

According to Magnus-Levy, 60 gm. of β-oxybutyric acid may be excreted when diabetic coma is not present, while in coma daily amounts of over 150 gm. have been observed. The percentage found by Magnus-Levy in diabetic urine rarely exceeded 0.5 to 1 per cent.

The best indirect method for the clinical purposes is the estimation of ammonia. This, of course, merely gives an idea of the amount of acids in the urine.

QUANTITATIVE ESTIMATION OF THE AMOUNT OF ACETONE IN THE URINE

By the Estimation of Iodoform.—As acetonuria accompanies a diabetic acidosis, the estimation of acetone and β-oxybutyric acid is of importance.

Acetone Estimation[3] *According to Hilger and Krämer.*—The method consists in weighing the iodoform produced in Lieben's reaction. One hundred cc. of urine are distilled, using an efficient condenser until 90 cc. have come over. The distillate is treated with a considerable excess of sodium hydroxid and iodopotassium iodid. (See p. 600, Lieben's Reaction.) The precipitate of iodoform is allowed to stand twenty-four hours and then is filtered through a tared filter. It is washed with a little cold water and dried over sulphuric acid in a desiccator. It is then weighed. A glass-wool filter is to be recommended, for then the washing is complete with very little water. The water adhering to the glass-wool is removed by suction and drying

[1] Ergeb. d. inn. med. Kinderheilk., 1908.

[2] If a brown residue remain in the flask, it is neglected. It contains hippuric acid that does not dissolve in the ether. As a small amount of β-oxybutyric acid may be included in the residue, it is dissolved in water, and added to the urine and reëxtracted.

[3] Huppert, Harnanalyse, 1898.

completed over sulphuric acid. One gm. of iodoform corresponds to 0.147 gm. of acetone.

It is simpler to extract the iodoform with ether. In the vessel in which the reaction has taken place one pours 20 cc. of alcohol-free ether. The contents of the vessel are well shaken and 10 cc. pipeted off. This is allowed to evaporate in a weighed dish. The residue is dried over sulphuric acid and weighed.

Messinger and Huppert estimate the amount of iodoform produced volumetrically.

Twenty cc. (with urine poor in acetone, 100 cc.), and distilled with 2 cc. of acetic acid 50 per cent. The distillate is redistilled after the addition of 1 cc. of sulphuric acid (1:8). The distillate is treated with an excess of decinormal iodin solution[1] and sodium hydroxid in excess. After standing a little while the excess of iodin is estimated with decinormal sodium thiosulphate solution. The details of the methods are given in Neubauer and Vogel, Harnanalyse, 0898. Magnus-Levy points out (Ergebnisse der inneren Medizin und Kinderheilkunde) that both the decinormal iodin solution and the sodium thiosulphate solution are liable to change their strength, so that frequent controls of the strength of the solutions should be made.

Acetone and aceto-acetic acid usually occur together in the urine; hence the iodoform obtained includes not only that derived from the preformed acetone, but also that derived from the acetone formed from the diacetic acid by the distillation. Acetone and aceto-acetic acid are about equally valuable in diagnosis (see p. 598), so this is no particular disadvantage. Besides, as we have no exact method of determining the amount of aceto-acetic acid, the estimation of the acetone is the only way in which we can obtain an approximate idea of the amount of aceto-acetic acid.

If one wishes to estimate the preformed acetone, this may be done according to Embden[2] or to Folin[3] by taking the acetone out of the solution containing it by means of a current of air. Magnus-Levy is not certain that in this method, for the performance of which Folin gives special directions, a certain amount of aceto-acetic acid is not converted into acetone.

ESTIMATION OF ACETONE ACCORDING TO ECKENSTEIN AND BLANKSMA

This method has been reported upon by S. Möller at P. Bergell's suggestion. It gives good results for clinical purposes.

Two hundred cc. of urine are distilled after adding 5 cc. of 33 per cent. sulphuric acid. The distillation takes about forty-five minutes. To the distillate, which will usually be about 100 to 120 cc., 0.5 to 1 gm. of paranitrophenylhydrazin, dissolved in 5 to 10 cc. of glacial acetic acid, are added. The mixture is diluted with 2 volumes of water. This amount is sufficient for all but exceptional cases of diabetes. It may be necessary to filter the solution of the hydrazone before it is added to the

[1] The requisite solutions are prepared in the following way: Decinormal iodin solution is obtained by dissolving 12.7 gm. of iodin and 20 gm. of potassium iodid in water and diluting to 1000 cc. The solution is so prepared that 10 cc. of the solution are decolorized by 10 cc. of decinormal sodium thiosulphate solution. Starch paste is used as an indicator. Decinormal sodium thiosulphate solution is prepared by dissolving 25 gm. of the crystalline salt (1000 cc. = 24.83 $Na_2S_2O_3 + 5H_2O$). The thiosulphate solution is titrated with decinormal potassium dichromate in the following way: A solution of 1 gm. of potassium iodid in 5 cc. of water and 2 cc. of 25 per cent. hydrochloric acid is treated with 10 cc. of decinormal potassium dichromate. The resulting mixture is diluted to 200 cc. with water, a little starch paste added, and titrated with the sodium thiosulphate solution. If the solution is exactly decinormal, 10 cc. of thiosulphate are necessary to discharge the blue color. If less be used, the thiosulphate solution must be diluted to the proper concentration or a factor used.

[2] Verhandl. Cong. f. inn. Med., 1907. [3] Jour. Biol. Chem., 1907, iii, p. 177.

urine. After some minutes, in the presence of acetone, a crystalline precipitate is formed. The precipitation is complete in half an hour, and longer standing should be avoided. The precipitate is filtered off on a hardened tared filter, dried to constant weight at 80° C., and weighed. The amount of precipitate obtained multiplied by 0.3 gives the amount of acetone. According to Möller, 0.006 gm. of the hydrazone remain in every 100 cc. of filtrate. As this equals 0.0018 gm. of acetone, a correction for this solubility must be made. Möller regards this method as the best for clinical purposes.

ESTIMATION OF ACETONE AND ACETO-ACETIC ACID ACCORDING TO FOLIN

[The same type of apparatus is used for this determination as in the Folin method for ammonia. (See p. 653.)

Into an areometer cylinder are introduced 20 to 25 cc. of the urine to be examined, 10 gm. of sodium chlorid, 10 drops of a 10 per cent. phosphoric acid solution, and a little kerosene oil. Into a gas absorption flask are introduced 150 cc. of water, 10 cc. of 40 per cent. potassium hydroxid solution, and a definite volume of decinormal iodin solution. The cylinder and the absorption flask are connected up in series as in the ammonia method, and a current of air drawn through. The acetone is removed from the urine saturated with sodium chlorid by the air current and is drawn into the alkaline iodin solution, where it is converted into iodoform. The time taken by this operation is twenty-five minutes. To the mixture in the absorption flask are added 10 cc. of concentrated hydrochloric acid, and the excess of iodin titrated with decinormal sodium thiosulphate and starch.

Aceto-acetic Acid.—The combined acetone and aceto-acetic acid may be determined by the Huppert-Messinger method, and the acetone found by Folin's method subtracted from this value. The difference gives the amount of acetone due to aceto-acetic acid.

ESTIMATION OF β-OXYBUTYRIC ACID ACCORDING TO SHAFFER

Introduce into a 500-cc. volumetric flask 25 to 250 cc. of the urine to be examined. The amount of urine used will depend upon the amount of β-oxybutyric acid which is contained in it. In the case of urines giving a strong ferric chlorid reaction, 25 to 50 cc. of urine will suffice. It is desirable to use such a volume of urine as will give 25 to 50 mg. of acetone. To the urine is added an excess of basic lead acetate and 10 cc. of ammonium hydroxid. It is necessary to be sure that an excess of the lead salt has been added. The mixture is made up to the 500 cc. mark, shaken thoroughly and filtered through a dry filter-paper; 200 cc. of the filtrate are distilled after the addition of 300 to 400 cc. of water and 15 cc. of concentrated sulphuric acid and a little talcum to prevent bumping. About 200 to 250 cc. of distillate are collected. This distillate contains, in addition to acetone from the preformed acetone and aceto-acetic acid, certain volatile acids. If it be made slightly alkaline, and a second distillation made, the distillate will contain all the acetone from acetone and aceto-acetic acid, and may be estimated by the iodin method.

The residue from the urine containing the sulphuric acid contains all the β-oxybutyric acid, and must now be converted by this oxidation into acetone. The residue is diluted and 0.5 gm. of potassium dichromate added. It is then distilled from a flask provided with a dropping funnel, and water added gradually to make up for the amount distilled over. Instead of water, one may use a 0.5 per cent. solution of

potassium dichromate. After about 500 cc. of distillate have been collected, the distillate is redistilled, after the addition of 20 cc. of 3 per cent. hydrogen dioxid and sufficient potassium hydroxid to make the solution alkaline. Collect 300 cc. of distillate and estimate the amount of acetone with iodin and thiosulphate; 1 mg. of acetone is equivalent to 1.794 mg. of β-oxybutyric acid.

The above methods for the determination of acetone, aceto-acetic acid, and β-oxybutyric acid are more accurate than any others that have hitherto been described, and should be used for the study of the clinical problem of acidosis.—C. G. L. W.]

ESTIMATION OF THE TOTAL DRIED RESIDUE OF URINE

Sometimes this is of clinical interest. The author has demonstrated that a watery diuresis—*i. e.*, diuresis produced by an increased consumption of water, more especially from a subcutaneous or intravenous infusion of salt solution—will increase the twenty-four-hour excretion of solids in the urine. The method of determination is very simple. Fifty cc. of urine are measured into a weighed dish and evaporated to a syrupy consistence over a water-bath at a very moderate temperature (not over 60° C.), after adding 2 or 3 drops of acetic acid, then dried further in a vacuum over sulphuric acid to a uniform weight. The urine must not be heated above 60° C., as otherwise ammonia will be given off from the urea. The addition of acetic acid is necessary to combine with any ammonia which may have been liberated in spite of the care taken when evaporating.

It is still safer to dry entirely in a vacuum without heating, but then a much smaller amount of urine (at most, 5 cc.) should be employed. A drop of acetic acid is added to the urine in a very shallow dish, along with a generous amount of sulphuric acid, and it is then allowed to dry in the vacuum to an absolute weight. If necessary, the sulphuric acid can be replenished and the vacuum restored by repeated exhaustion.

An approximate estimation of the total amount of solids in 1 liter of urine can be obtained from the specific gravity of the urine. (See p. 551.)

URINARY ACIDIMETRY AND ALKALIMETRY

(Determination of Acidity and Alkalinity. Estimation of the Acidic and Basic Points.)

The conditions which affect the reaction of the urine have already been discussed upon p. 556 et seq. The reaction of individual specimens of urine varies; hence the degree of acidity must be determined from a specimen of the mixed twenty-four-hour urine. The addition of a few drops of chloroform, or keeping the urine upon ice, will prevent any change in the reaction due to decomposition.

The quantitative estimation of the reaction by means of acidimetry or alkalimetry is accomplished by titration. Certain objections have been constantly raised in reference to the possibility of titrating the acidity of the urine, and these objections have also been fully considered in Nägeli's[1] experiments upon this subject, which were undertaken at the author's request. The author fully realizes the theoretic justification of all these objections, which arise from the fact that the end-reactions of the titration of the phosphoric acid are theoretically never distinct, and not always so even from a practical standpoint. The reasons for this fact have been clearly explained by T. Heffter.[2] So long as the chemist gives us nothing better, however, we are forced to use these methods in practice, even though they are not strictly accurate, and Nägeli has at least shown that it is possible to obtain approximate values for the acidity of the urine by means of titration.

In view of the undeniable difficulties of titrating the urine acidimetrically, the author thinks it is entirely beside the mark to attempt to replace the classic conception of acidity by an entirely different one—namely, the concentration of the hydrogen ions—instead of trying to improve the method of titration. The acidity is not due to the concentration of the hydrogen ions, but to the number

[1] Zur Aciditätsbestimmung des Urines, Zeit. f. physiol. Chemie, vol. xxx, parts 3, 4, and 5, p. 366.

[2] Ergebnisse der Physiol., I. Jahrg., 1902.

of hydrogen atoms capable of being replaced by metals and contained in a given quantity of a fluid. These are entirely different conceptions, and, since the old conception of acidity is still upheld by the teachings of physical chemistry, nothing but confusion can result from the substitution of a new conception.

It would lead to a very distinct confusion in ideas if the conception of neutrality were introduced, depending on the behavior of the urine to gas-electrodes, and, therefore, on the concentration of hydrogen ions in the solution.

Nägeli tested a large number of indicators in reference to their behavior toward the more important salts occurring in the urine, and ascertained how much information could be obtained from them by any change of color they might undergo upon titration with an alkali or an acid, in reference to the chemical saturation of the acidic or basic affinities of the urine. The following discussion gives the essential results and conclusions obtained by Nägeli.

Only two reagents, phenolphthalein and alizarin red,[1] are of any value for the purpose under discussion. Litmus is absolutely useless; it never shows any sharp change of color when titrating phosphates. When phenolphthalein is used, the end-reaction is indicated by the bright-red color shown by this indicator when the acid solution becomes alkaline on the addition of $\frac{N}{10}$ sodium hydroxid solution. (For preparation see p. 453.) When alizarin red is employed, the change from red to yellow indicates the end-reaction which takes place upon adding $\frac{N}{10}$ hydrochloric acid (for preparation, see p. 453) to an alkaline solution the moment free acid is present. Alizarin red does not react to acid salts nor to CO_2. The following table indicates best how the most important constituents of the urine react on titration toward the above indicators:

Titration with phenolphthalein and $\frac{N}{10}$ NaOH.		Yellow as soon as free HCl is present.
		Acidic point.
Colorless as long as are present:	NaH_2PO_4, KH_2PO_4, $NH_4H_2PO_4$, $Ca(H_2PO_4)_2$ H_2CO_3 (carbonic acid)	Red. Titration with alizarin red and $\frac{N}{10}$ HCl.
Neutral point: Red as soon as NaOH changes all to:	Na_2HPO_4, Ka_2HPO_4, $(NH_4)_2HPO_4$, $CaHPO_4$, $NaHCO_3$, $KaHCO_3$	
Basic point: (free alkali) not determinable.		

Urea, chlorids, sulphates, urates, oxalates, kreatinin, *et al.*, remain indifferent to titration, but, on account of their small quantity, they are unimportant.

The above table shows that titration of urine with sodium hydroxid and phenolphthalein to determine the point of neutralization gives valuable information as to acid affinities and acid equivalents. The value found, usually expressed in cubic centimeters of $\frac{N}{10}$ sodium hydroxid, is often termed the acidity of urine. This does not, of course, indicate the amount of acid excretion, but only how much the acid equivalents contained in the urine exceed the basic equivalents. The amount of acids in the form of neutral salts (NaCl) or salts reacting alkaline to phenolphthalein (Na_2HPO_4) is, of course, not included in the acidity. Besides this, it should be remembered that, when titrating with phenolphthalein, the neutral point is placed where all phosphates are transformed into secondary salts corresponding to the formula Na_2HPO_4, and the H_2CO_3 is changed to $NaHCO_3$. In this sense the acidity is not identical with the basic capacity, because phosphates with the formula Na_2HPO_4 can still take up one more basic atom. The basic point —*i. e.*, the moment Na_2HPO_4 is changed to Na_3PO_4 by the addition of NaOH and free alkali becomes present—cannot be determined by any indicator.

By titration with $\frac{N}{10}$ HCl and alizarin red one obtains in a similar manner information as to the basic equivalents in the urine. Just as the acidity is measured with $\frac{N}{10}$ sodium hydroxid, the basicity is measured with $\frac{N}{10}$ HCl. The acidity

[1] Alizarin red of Merck (alizarin sodium sulphonate).

can be ascertained only to the neutral point, not to the basic point, whereas the total basicity may be determined, because the moment when free acid appears, following the addition of $\frac{N}{10}$ HCl (acid point), is indicated sharply by alizarin red.

Leaving out of consideration the urates and oxalates, the sum of the values, according to alizarin and phenolphthalein, corresponds, approximately to the contents of carbonic and phosphoric acid molecules in the urine. Finally, the two titrations give an insight as to the amount of the bases which are excreted combined with phosphoric acid. If the urates, oxalates, and carbonates are not considered, this amount is approximately obtained when the value of the phenolphthalein titration is added to double that of the alizarin titration. In the titration with phenolphthalein, as much alkali equivalent is added to complete the reaction as there is in the phosphates corresponding to the formula NaH_2PO_4 and appearing in the reaction; while in the alizarin reaction one-half as much acid equivalent must be added in order to bring about the end-reaction. This calculation contains considerable errors only when there are present in the urine relatively large quantities of carbonates, oxalates, or urates, which may enter into the reaction. This is seldom the case, however.

Urines which reacted alkaline to phenolphthalein could be titrated by means of $\frac{N}{10}$ HCl with the indicator and the neutralization point accurately determined if the alkalinity were caused by *fixed* alkalis. This condition, however, has never been observed. In general, a urine which reacts alkaline to phenolphthalein contains ammonium carbonate, and in this case the addition of $\frac{N}{10}$ HCl causes the formation of acid ammonium carbonate, which immediately decomposes and liberates CO_2 and NH_3. The indicator, being much more sensitive to CO_2 than to NH_3, becomes decolorized (by the CO_2) long before the NH_3 in the urine is completely neutralized—*i. e.*, before all the $(NH_4)_2NCO_3$ is transformed into $(NH_4)HCO_3$. The obtaining of an accurate end-reaction with phenolphthalein under these conditions is therefore impossible. Actually, however, this difficulty presents no serious disadvantage, because the ammoniacal character of urine, with the exception of the presence of ammonium carbamate as the result of calcium feeding, is caused exclusively by the bacterial decomposition of urine. In such cases quantitative determinations have no interest. On the other hand, it is to be emphasized that the determination of the acid point—*i. e.*, the point at which all the NH_4Cl is transformed into HCl—presents no difficulties. Such determinations acquire, under certain conditions, clinical interest in the consideration of the degree of bacterial decomposition of freshly voided urine in cystitis.

On the other hand, it is conceivable that titration with HCl in the presence of alizarin does not lead to accurate results if the urine contains large amounts of ammonium salts, as is the case in diabetic acidosis. Nägeli found in the titration of ammonium salts of dibasic acids—*e. g.*, ammonium oxalate with HCl—that the change of color of the alizarin into yellow does not take place at the moment of the appearance of free acid, but as soon as the acid salts are formed. The color-change is also too gradual to allow of sharp reading. Nevertheless, this disturbance of the reaction does not come into play in the case of a monobasic acid, such as β-oxybutyric. In the normal condition of the excreted ammonium salts, these hardly effect the determination of the acid point. In cases where the ammonium content of the urine is excessive, the determination of the acid point can be performed as follows: In a portion of the urine the ammonia is quantitatively determined according to the Schlösing method (p. 652), or that of Krüger and Reich or of Shaffer or Folin, and then to another portion is added the equivalent amount of NaOH, sufficient to set the NH_3 free. This ammonia can be driven off by heat, and the solution then titrated in the usual way.

In practice the titration is carried out in the following manner: To 2 portions of 10 cc. of the urine are added respectively phenolphthalein and alizarin. The first is titrated with $\frac{N}{10}$ NaOH to the appearance of a permanent red color. To the second, $\frac{N}{10}$ HCl is added until the red color has changed to yellow. The color of the urine itself does not interfere in the titration to any noticeable extent, especially if there is placed alongside of the beaker in which the titration is being performed a second, for control, with equal amounts of urine and indicator to which no acid or alkali is added. Both solutions should be diluted to an equal extent. Strongly colored urine can be diluted or be decolorized by animal charcoal which has been tested and found to be neutral. The charcoal should be repeatedly extracted with boiling water until the washings are neutral. Even then one is not certain in

the use of this reagent, for certain substances are absorbed. If the end-reaction is not sharp and the cause is to be ascribed to the presence of ammonium salts, then the latter may be estimated and replaced by an equivalent amount of a fixed alkali as before described. For the technic of titration and preparation or normal solutions see pp. 453 and 456. Proteins must be removed by heat and acetic acid, in which case a known amount of the acid should be added, and this taken into consideration in the titration. The values found in these titrations may be expressed in cubic centimeters of $\frac{N}{10}$ NaOH, or calculated in grams of NaOH (a $\frac{N}{10}$ NaOH solution contains in a liter 4 gm. of NaOH). Haig found that the average acidity of the daily urines of healthy persons equaled 5.5 gm. of oxalic acid or 3.5 gm. of NaOH. Späth, however, gives a daily acidity of 1.45 gm. of HCl, corresponding to 1.6 gm. of NaOH.

Freund has lately suggested, and Lieblein[1] has agreed with him, that the acidity of the urine can be estimated from the amount of acid phosphates, since the acid reaction of urine is due mainly to these salts.

Lieblein estimates in the usual way the total amount of phosphoric acid in a definite volume of urine by means of uranium nitrate. (Compare p. 648.) He then removes the secondary acid phosphate from an equal amount of urine by precipitation with barium chlorid, and titrates again the acid phosphates in the filtrate. Nägeli's researches have raised certain objections to this method, however.

Neumeister[2] suggests a method to prevent the phosphate from interfering with all acidity titrations. It is a modification of Maly's[3] old procedure. Fifty cc. of urine are rendered strongly alkaline by adding 25 cc. $\frac{N}{10}$ sodium hydroxid; the mixture is heated to boiling; 25 cc. of a barium chlorid solution sufficiently concentrated to precipitate all the phosphoric acid are then added. The resulting mixture is shaken, and 50 cc. are filtered through a dry filter (equal to 25 cc. of the urine); the filtrate is colored with phenolphthalein and then titrated with $\frac{N}{10}$ sulphuric acid to the appearance of a neutral reaction. The less sulphuric acid required, the stronger the acidity of the specimen of the urine.

Nägeli considers this modification of Maly's original method to be entirely unreliable (*loc. cit.*).

THE TITRATION OF FLUIDS WHICH, IN ADDITION TO PHOSPHORIC ACID SALTS, CONTAIN ALKALINE EARTHS AND AMMONIUM SALTS

Moritz[4] has suggested a method which, in addition, allows one to titrate the acidity of fluids containing the above-mentioned components without the objections which may be made to the method of Nägeli.

According to the investigations of Moritz, the difficulties in the estimation of the acidity of the urine and the gastric juice, using phenolphthalein as an indicator, are due to a zone of equilibrium, in which the reaction of the indicator is not sharp. The content in salts of ammonia also disturbs the reaction, so that, as the action of ammonia on phenolphthalein is weak, more alkali must be added than is actually necessary for complete neutrality. In consequence of the feeble alkalinity of the acid potassium and sodium carbonates, the carbonate titration is not sharp, and, finally, through the precipitation of basic salts of calcium, the mixture becomes apparently acid. Magnesium salts, on the other hand, do not produce this effect.

Moritz shows that the difficulties due to the presence of phosphates, ammonium salts, and carbonates may be completely removed when an equal volume of saturated sodium chlorid solution, freed from carbon dioxid by boiling, is added to the mixture to be titrated. The action of this salt is due to a decrease in the dissociation of the salts in solution. With this addition, solutions of alkaline carbonates are neutral to phenolphthalein. According to Moritz, when saturated sodium chlorid is added, the end-point occurs with phenolphthalein, at the boundary between the primary and secondary carbonates, with the phosphates at the boundary between the secondary and tertiary salts; the difficulty, which is due to the presence of calcium, is eliminated by precipitating the calcium salts by the titration. The process is as

[1] Freund, Centralbl. f. d. med. Wissenschaft, 1892, p. 689; Lieblein, Zeit. f. physiol. Chem., vol. xx, parts 1 and 2.

[2] Lehrbuch d. physiol. Chem., 1895, vol. ii, p. 225.

[3] Zeit. f. anal. Chem., vol. xv, p. 417.

[4] Arch. f. klin. Med., lxxx, No. 5 and 6.

follows: In an Erlenmeyer flask, holding 150 cc., are placed 10 cc. of the fluid to be examined, 4 cc. of seminormal sodium oxalate solution, and 15 cc. of concentrated sodium chlorid. After the addition of the oxalate, some time is allowed to elapse in order to complete the precipitation of the calcium oxalate. The sodium chlorid solution is then added. Two similar solutions are prepared, the one being used for a comparison. If this be done, the change in color, even in dark urines, is quite distinct. A special process is necessary for urines when a precipitate of phosphates takes place. The solution of the phosphates in standard hydrochloric acid can only be done when the urine contains no carbonates. If carbonates were present, the carbon dioxid would be evolved and the acidity would then appear too small.

If one has to do with carbonates in the urine, the precipitate must be collected on a filter, dissolved in a known volume of standard acid, using methyl-orange as an indicator, and after the addition of sodium oxalate and sodium chlorid, retitrated with standard alkali. The alkali equivalent of the precipitate must be added to that obtained with the filtered urine.

THE ESTIMATION OF ACIDITY OF THE URINE BY TITRATION

O. Folin has informed me that he had published a method of estimating the acidity in the urine by titration quite similar to that of Moritz one year before the latter's publication (American Journal of Physiology, July 1, 1903, No. 5). This author too makes use of an oxalate, namely, oxalate of potassium, in order to prevent the formation of basic calcium phosphate during the titration, the principle of this method having been mentioned by Liebig and used since by Jäger.[1]

He makes use of the same salt to avoid the difficulties arising from the presence of ammonia salts in the urine. Moritz employed for this purpose concentrated solutions of sodium chlorid. Folin, on the other hand, simply adds an excess of potassium oxalate, which, of course, exerts an action similar to that of the sodium chlorid. Folin has found that after the addition of an excess of potassium oxalate during the titration of acid fluids, almost the same quantities of alkali are necessary to produce a change of color in phenolphthalein as has been theoretically worked out, even though the fluids in question contain large amounts of ammonia salts; if the potassium oxalate is not added, on the other hand, the presence of ammonia salts leads to a marked difference in the amount of alkali necessary to produce the change in the color of the indicator.

Folin's method of estimating the total acidity of human urine is as follows: 25 cc. of urine are measured out with a pipet into an Erlenmeyer flask of 200-cc. capacity. To this are added 2 or 3 drops of 1 to 2 per cent. solution of phenolphthalein and 15 to 20 gm. of powdered neutral potassium oxalate. The mixture is shaken for about one minute and then immediately titrated with a decinormal solution of sodium hydroxid until the appearance of a weak but distinct rosy tint. The flasks ought to be shaken during the titration in order to keep the fluid as perfectly saturated with the oxalate as possible.

FOLIN'S METHOD OF ESTIMATING THE ACIDITY OF THE URINE DUE TO ORGANIC ACIDS. (The Content of Urine in Organic Acids.)

In a second noteworthy paper published in the American Journal of Physiology, 1905, No. 1, p. 102, Folin brings forth a great deal of evidence showing that in spite of traditionally accepted assumption phosphoric acid does not exist in the urine in the form of a mixture of dibasic and monobasic phosphates, but only as a monobasic phosphate. Moreover, the total acidity of the urine is greater than that

[1] Centralbl. f. d. med. Wissen., 1902, p. 641.

caused by the presence of the acid phosphate, for a certain amount of it is due to the presence of organic acids. If this assumption be correct,—and in my opinion Folin's evidence is quite convincing,—the estimation of the acidity caused by the organic acids as compared with that due to mineral acids is of great clinical importance. In the first paper of Folin's, mentioned above, he described a somewhat complicated procedure for estimating the acidity of the urine due to mineral acids. By subtracting the values obtained by this method, which we shall not further describe in this place, from the figures giving the total acidity of the urine, one is enabled to find the acidity due to the presence of free organic acids.

CRYOSCOPY OF THE URINE; OSMOTIC PRESSURE OR THE MOLECULAR CONCENTRATION OF THE URINE

PREFATORY NOTES

According to van t'Hoff, substances held in solution act like gases, and this observer has shown that the laws of Boyle-Mariotte, Gay-Lussac, and Avogadro apply to these substances as well as they do to gases. The dissolved molecules behave exactly like the molecules of a gas, which exert a pressure upon the wall of the containing vessel by their endeavor to diffuse themselves through the greatest possible space. This pressure of dissolved molecules is the osmotic pressure, and this pressure, according to van t'Hoff, corresponds to the pressure which the dissolved substance would exert as gas or vapor of the same molecular concentration and in the same space. From this it follows that osmotic pressure shows the same dependence upon the temperature as does the pressure of a gas, according to the law of Gay-Lussac, and also that solutions which contain the same number of molecules in the same volume of fluid possess the same osmotic pressure, just as gases, according to Avogadro's law, exert the same pressure when they contain the same number of molecules in the same space. If we apply the law of gases to solutions, it will also be found that just as every gram molecule or "mol" of a gas—*i. e.*, the quantity which weighs as many grams as there are units in the molecular weight—in a space equivalent to 22.4 liters at 0° C. exerts a pressure of one atmosphere, so also that solutions which contain 1 gram molecule of substance dissolved in 22.4 liters of fluid possess an osmotic pressure of one atmosphere. Vice versâ, if 1 gram molecule be dissolved in a liter of water, the osmotic pressure, corresponding to Mariotte's law, will be 22.4 atmospheres. From this it will also be observed that the osmotic pressure is directly proportional to the concentration. A 1 per cent. sugar solution, for example, possesses double the osmotic pressure of a 0.5 per cent. solution. These laws, however, apply only to solutions of non-electrolytes. Electrolytic substances, such as acids, bases, and salts, when in solution, are partly dissociated into ions, and a comparison of the osmotic pressure with the concentration of the ions shows that in such solutions the osmotic pressure is affected by the ions, just as it is by the molecules (Arrhenius, van t'Hoff). The osmotic pressure of a partly dissociated solution is consequently proportional to the sum of the undissociated molecules and of the ions. The osmotic pressure of a 0.5 per cent. solution of sodium chlorid, unlike that of a sugar solution of corresponding strength, is more than half of the osmotic pressure of a 1 per cent. solution, because dilute solutions are more strongly dissociated and contain proportionately more ions than do concentrated solutions.

Under ordinary conditions, osmotic pressure has as little visible effect as has the pressure of a gas confined within a vessel. We can, however, demonstrate the effect of osmotic pressure by carrying out certain experiments. For example, if we place a watery solution of a substance in a vessel with membranous, yielding walls which will allow the passage to water, but not to the dissolved substance, in other words, a "semipermeable" membrane, and place this closed vessel in water, the dissolved molecules will become separated in proportion to the amount of water which penetrates the membrane from without. By this means the osmotic pressure becomes manifest, and there is a distention of the elastic vessel, an effect of pressure in the ordinary sense of the word. The latter phenomenon has also been designated as a result of the "attraction of the solution for water": this is readily understood, but it does not indicate the theoretic point involved. The amount of this "attraction" is equal to the osmotic pressure, since equilibrium is not established in any

experiment until the hydraulic pressure has become equal to the osmotic pressure. The osmotic pressure of a watery solution may consequently be measured hydraulically by placing the particular solution in a tube, the lower end of which is closed by a membrane that allows the water, but not the dissolved substance, to pass through it, and then placing the lower portion of this tube in a vessel of distilled water. The water passes into the tube through the pores of the membrane, and the solution continues to be diluted until the hydrostatic pressure in the tube becomes equal to the osmotic pressure of the original solution. In this experiment the final height of the column of fluid is consequently the measure of the osmotic pressure, and the latter may be correspondingly expressed in atmospheres. This method, however, in actual practice is not easy, and the osmotic pressure of solutions is usually determined in another manner, as will presently be shown.

METHOD OF DETERMINING THE FREEZING-POINT

In medicine we are chiefly concerned with the determination of the osmotic pressure of the blood and of the urine, more rarely with that of other fluids of the body. The best method for this purpose, and the one which is almost exclusively employed, is the method of determining the freezing-point, or cryoscopy. The method depends upon the fact, discovered by Raoult, that the lowering of the freezing-point of a watery solution, as compared with the freezing-point of distilled water, is proportional to the molecular concentration of the solution—*i. e.*, to the number of molecules contained in a unit of volume, and consequently (see above) to the osmotic pressure. We must, nevertheless, remember the fact, pointed out by Arrhenius and van t'Hoff, that in partly dissociated solutions the ions have the same values as the undivided molecules in determining osmotic pressure, and consequently in the lowering of the freezing-point. It will be seen from what has been said that if one watery solution has a freezing-point of $-1°$ C., and another has one of $-0.5°$ C., then the first solution possesses double the osmotic pressure of the second. The lowering of the freezing-point is usually designated by Δ, and the minus sign is omitted. A solution which freezes at $-1°$ C. consequently has a lowering of the freezing-point, $\Delta = 1$. From the previously stated fact, that a gram-molecule dissolved in a liter of water has an osmotic pressure of 22.4 atmospheres, it is easy to estimate the osmotic pressure in atmospheres from the lowering of the freezing-point. Since a gram-molecule dissolved in a liter of water produces a lowering of the freezing-point indicated by $\Delta = 1.85$, it follows that a lowering of the freezing-point of 1.85 corresponds to an osmotic pressure of 22.4 atmospheres. Moreover, since the lowering of the freezing-point and the osmotic pressure vary proportionately, the correct osmotic pressure of any solution may be estimated in atmospheres from the freezing-point of the solution. The blood, for example, has an osmotic pressure of about 7 atmospheres. From a medical standpoint, however, we are more interested in the deviation of the fluid examined from the normal—*i. e.*, in a relative value—and consequently the freezing-point is not usually calculated in pressure values, but the osmotic pressure is simply indicated by the lowering of the freezing-point.

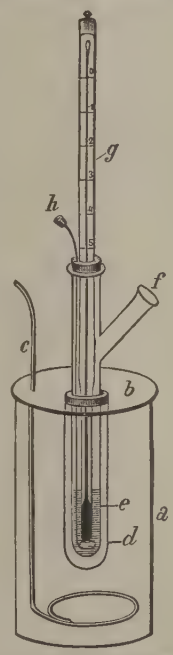


Fig. 252.—Beckmann-Heidenhain's apparatus for determining the freezing-point of a solution

The freezing-point is usually determined by means of Beckmann's apparatus, Heidenhain's modification of which is shown in Fig. 252.[1] The instrument is

[1] Recently it has been suggested to use the cold produced by the evaporation of a volatile liquid, such as ether. The evaporation is hastened by means of a foot-bellows. The apparatus constructed by Röthlisberger, in Baden, seems to be more convenient. In this apparatus the air-current is produced by means of a water suction-pump. The current may be so regulated that practically a constant temperature is produced. (See Röthlisberger, Münch. med. Woch., 1905, No. 22.) The apparatus may be obtained from M. Schärer, A. G., Bern. It costs 65 francs.

composed of the following parts: *a* is a battery jar, which has a metal cover (*b*), perforated in the middle. This jar holds the freezing-mixture, which may be stirred by the strong wire loop (*c*). The opening in the lids gives passage to the wide reagent glass (*d*), in which the actual freezing-vessel (*e*) is held in place by a perforated cork. This freezing-vessel has a lateral prolongation (*f*), the importance of which for the "inoculation of the fluid" will subsequently be pointed out. Between the vessels *d* and *e* there is an inclosed layer of air, which is for the purpose of allowing the cold to act gradually upon the fluid contained in *e*. The thermometer (*g*), divided into hundredths of a degree, is held in the freezing-vessel by means of a perforated cork, which also gives passage to the platinum-wire stirrer (*h*). The thermometer of the original apparatus does not possess a fixed zero, since in purely physical experiments it must be used not only for watery, but also for other, solutions having an entirely different freezing-point. By a special manipulation, the details of which may be omitted, the amount of mercury in the thermometer may be increased or diminished from a specially constructed reservoir at the top of the thermometer, so that the freezing-point of the particular solvent can be brought within the scale. The freezing-point of the pure solvent is first determined, and then that of the solution. The difference obtained is the lowering of the freezing-point in hundredths of a degree.

This procedure with the original instrument of Beckmann is too complicated for clinical purposes, and, as we have to do with watery solutions only, we now usually employ a thermometer with a fixed zero (Heidenhain), which is found at the upper end of the scale, and corresponds to the freezing-point of pure distilled water (see figure). Below this point the scale is divided into hundredths of a degree. The upper end of the capillary thermometer tube is expanded, so that when the instrument is exposed to higher external temperatures, the mercury may accumulate in this expansion and not break the tube. An accurately made instrument of excellent quality and adapted for clinical purposes may be obtained from the glass instrument factory of Götze, Hertelstrasse 4, Leipsic. At the author's request this firm has supplied an instrument with which only 5 cc. of fluid are necessary, in order to determine the freezing-point. This is a matter of great importance, since we frequently have to do with a very small quantity of fluid, particularly in the examination of the blood.

Since, in time, all thermometers vary, it is important to test the accuracy of the zero mark occasionally, even though the scale were originally absolutely correct. This is done by determining the freezing-point of distilled water with the instrument, and, when it does not agree exactly with the zero mark, adding the correction to all subsequent readings. In doing this, however, we cannot employ any distilled water at random. After a time distilled water absorbs gases, and it also takes up a certain amount of alkali from the glass container; this is sufficient to cause a distinct lowering of the freezing-point. For this reason the distilled water employed must, at least, be freshly boiled or, better still, freshly distilled. In this distillation the receiver should consist of a so-called steamed flask, *i. e.*, one which has been freed from soluble alkali by means of a current of steam.[1] If it be desired to verify not only the zero mark, which may change through no fault of the maker of the instrument, but also the accuracy of the scale, this may be done by also determining the freezing-point of a pure 1 per cent. sodium chlorid solution. According to Hamburger, the freezing-point of such a solution is 0.589. If the instrument be correct, this is the value which should be found after making the necessary correction for the zero mark.

In the determination of every freezing-point, care must be exercised to see that small particles of mercury are not sticking to the sides of the upper expanded portion of the thermometer, since, if this were the case, an error would arise from the exclusion of this part of the mercury. For this reason the expansion should be examined with a lens before every determination, and if separate particles of mercury are found, they must be united with the mercurial column, either by shaking or by warming the instrument.

In determining a freezing-point the jar (*a*) is first filled with a freezing mixture. In order to obtain correct results, it is important that the freezing mixture be correctly prepared. It should not be too cold. The best mixture, according to Hamburger,[2] is one of 3 parts of finely cracked ice or snow with 1 part of sodium chlorid; this is placed in the jar, and sufficient water added to make the temperature about −3° C. If the temperature rises in the course of the experiment, a fresh

[1] See Cohen, Vorträge über physikalische Chemie, 1902, second ed., p. 11.
[2] Osmotischer Druck und Ionenlehre, 1902.

amount of ice and sodium chlorid in the given proportion should be added. If Röthlisberger's apparatus is used, where cold is produced by the evaporation of ether or carbon disulphid, the current of air is so regulated as to produce the required temperature. The fluid to be examined is now placed in the freezing-tube, and the thermometer and the platinum stirrer subsequently introduced. Care must be taken that the mercury reservoir of the thermometer is completely surrounded by the fluid, so that it is entirely submerged, and does not come in contact with any portion of the freezing-tube. The freezing-tube is then inserted into the reagent glass in the cover of the battery jar, so that it is surrounded by a uniform layer of air. The fluid in the freezing-tube must be kept in constant motion by gentle, but interrupted, movements of the platinum stirrer (*h*). The fluid must not splash. The mercury soon commences to sink in the thermometer, leaves the upper expanded portion, enters the capillary tube, and quickly falls to a point more or less below the freezing-point (excessive cooling), and then suddenly rises to a definite point, at which it remains stationary for some time. This point is the freezing-point of the fluid examined, and is read off. At this time needles of ice commence to form in the fluid, and it gradually becomes solidly frozen. When this has happened, the mercury commences to descend again. This complete freezing should not be waited for, however, but the determination should be repeated immediately after the mercury has ceased to ascend, by taking out the freezing-vessel, holding it in the hand, and stirring the fluid constantly until the mercury commences to ascend, when the freezing-vessel is again introduced into the reagent glass (*d*), and the freezing-point again determined as before. In warming the freezing-vessel for the purpose of repeating the determination all the crystals should not be melted—*i. e.*, the temperature must not reach 0° (since the crystals consist of pure water)—because errors would arise if the fluid were subsequently "inoculated" with small pieces of ice (see below). When three determinations have been made, one immediately after the other, the average of the three is taken as the final result.

In order to determine correctly the freezing-point it is important to avoid excessive cooling (see above), since large masses of ice will form, and as these consist of pure water, a more concentrated solution remains, which gives a lower freezing-point corresponding to its higher osmotic pressure. The error of excessive cooling is avoided, first of all, by compounding the freezing-mixture so that its temperature is not too low. The safest way would be to compound it so that its temperature would be but a few tenths of a degree below the expected freezing-point, which could be approximately determined in a preliminary experiment. This takes up too much time, however, since the cooling would proceed so slowly, and in addition it makes the necessary recognition of the descent and ascent of the mercury much more difficult. If the temperature of the freezing mixture be −3° C., instead of the very low temperatures so commonly employed previously, the chances of excessive cooling are considerably reduced. An additional means of avoiding excessive cooling consists of the introduction of a minute piece of ice into the fluid through the lateral prolongation at the moment when the mercury falls below the zero-point. In physical chemistry this is referred to as "inoculation" of the fluid with a piece of ice. This accelerates the formation of ice, and consequently diminishes the danger of excessive cooling. This would seem to dilute the solution, and consequently lead to false results; but this is not the case when the manipulation is correctly performed, because the piece of ice cannot melt if the temperature be below zero. This would be possible, however, if the fluid were warmed in the hand to the zero point in making the second and third determinations. This must be avoided, as has been previously pointed out, and no error will then result if the fluid be repeatedly "inoculated." It will readily be understood that the fluid is useless for subsequent determinations after it has become thoroughly melted. In the author's experience he has found that "inoculation" is necessary if the temperature of the freezing-mixture be not more than 3° C. below the expected freezing-point, since in this manner the excessive cooling is avoided.

EMPLOYMENT OF CRYOSCOPY FOR THE STUDY OF THE RENAL FUNCTIONS

Since the determination of the freezing-point furnishes us with a simple and clinically applicable method of estimating the osmotic pressure, and consequently the molecular concentration of a fluid, this method of examination has been applied to the urine and to the study of the functions of the kidney. By this method it has been attempted to determine not only the total amount of work done by both kidneys, but also, by the practice of ureteral catheterization or by Luys' method of separation of the urines (see p. 558 et seq.), to compare the functions of the two

kidneys. Disregarding the excretion of water, which is doubtless a renal function and not to be regarded simply as a filtration, it is clear that the greater part of the work of the kidney consists of excreting a fluid of high osmotic pressure from the blood, which has a much lower molecular concentration. An expenditure of energy is necessary for this purpose, and the production of a urine of high osmotic pressure is consequently to be regarded as an accumulation of potential energy. Should we assume, as is frequently done, that this production of a fluid of higher osmotic pressure from the blood represents the entire work of the kidney, the daily amount of work done by both kidneys would be calculated by $W = Q(\Delta - \delta)$, in which Q is the daily excretion of urine, Δ the freezing-point of the urine, and δ that of the blood. The result may be designated as the daily osmotic capability of the kidney. It should be remembered, however, that this measure of the renal functions is neither complete nor exact. It is not complete, because it neglects the work done by the kidneys in excreting water, and also because it is evident that by the excretion of a diluted urine, which has a lower osmotic pressure than that of the blood, and in which the kidneys create no osmotic pressure whatever, the kidneys still perform work that is not apparent as osmotic pressure.[1] It is not exact, since we do not know that different molecules require the same amount of energy for their excretion. Although the difference in the molecules is immaterial for the calculation of the potential energy stored up in the urine, it is not only plausible, but also possible, that the excretion of a molecule of sodium chlorid requires a different expenditure of energy than is necessary for the excretion of a molecule of urea. The difference probably exists in variations in the amount of heat evolved, and is not at all apparent in the osmotic pressure of the urine. The majority of the works upon cryoscopy of the urine do not regard this point at all, and consequently deduce far-reaching conclusions from the determination of the freezing-point of the urine which are by no means justified.

The utilization of the results of cryoscopy for the determination of the functional activity of the kidneys is also complicated by difficulties which are encountered in the study both of the mixed twenty-four-hour urine and of the separately collected urine from each kidney. It is difficult to deduce conclusions from the freezing-point of the mixed twenty-four-hour urine, since this freezing-point is subject to great variations under normal conditions. It is not unusual for the lowering of the freezing-point of the twenty-four-hour urine to exhibit a physiologic variation of from 0.9° to 2.7° C., and still greater variations may be encountered under perfectly normal conditions, dependent upon the ingestion of food and water. If an individual drink

[1] Should we assume that the production of an osmotic pressure in the urine exceeding that of the blood is the only work done by the kidneys, as is frequently stated, we should arrive at the paradoxic and ridiculous conclusion that kidneys which furnish a diluted urine perform no work at all, or even a negative amount of work (the latter if $\Delta - \delta$ is negative), while on account of the markedly increased quantity of water in the urine in these cases, a particularly large amount of work is perhaps represented.

The author's opinion, that the excretion of water by the kidney is a specific function of this organ, will possibly be objected to on the ground that this excretion can be accounted for by assuming that the secreting membranes of the kidney are extremely permeable to water, and that it is not at all necessary for the kidney to supply energy for a simple filtration. Such a permeability to water, however, must be something quite specific, since a similar permeability is found nowhere else in the body. We also have reason to believe that this excretion of water is an active function, since under physiologic conditions it is always accurately adapted to the needs of the organism. A further proof of the activity of the kidneys in excreting water is furnished by the hypertrophied kidneys of beer-drinkers, which, by their differences from the kidneys of wine-drinkers, demonstrate that the hypertrophy is due to the effect of water and not to that of alcohol. The same thing is still more strikingly shown by the renal hypertrophy acquired in diabetes insipidus. If the activity of the kidneys were not increased under these conditions, they would not become hypertrophic.

Another reason for the author's opinion that the so-called osmotic energy of the kidneys is no accurate measure for the work done by these organs is the fact that the ionization of the urinary constituents varies with the concentration of the urine. Since part of this ionization occurs after passing through the renal epithelium (in case a concentrated urine become more dilute), this portion of the osmotic pressure dependent upon ions, or at least some of it, cannot be reckoned as work done by the kidney.

large quantities of water, the difference between the freezing-point of the urine and that of distilled water may amount only to 0.11° C. (Köppe). In nursing infants the osmotic pressure of the urine is always less than that of the blood, and the lowering of the freezing-point may vary between 0.087° and 0.455° (Köppe). In any individual case the freezing-point may vary from day to day. Since there is no normal freezing-point for normal urine, we can draw conclusions in reference to the renal function in pathologic cases only when repeated examinations have shown the freezing-point to be constantly too high or too low, and when this extreme variation cannot be accounted for by anomalies in the ingestion of food or water. These difficulties are by no means overcome by basing the calculation upon the daily osmotic energy of the kidneys determined by $W = Q(\Delta - \delta)$ instead of upon the lowering of the freezing-point (Δ) or by employing the product of the daily excretion and the freezing-point of the urine ($Q - \Delta$). The formula $W = Q(\Delta - \delta)$ is more exact than the freezing-point alone, since it not only indicates the molecular concentration, but also measures the osmotic energy expended by the kidneys within twenty-four hours, while the product $Q\,\delta$ is a measure for the number of molecules excreted in a similar period of time. The previously emphasized objections to utilizing the freezing-point also exist here, since under normal conditions the number of excreted molecules and the product $Q\,\delta$ vary just as much as does the molecular concentration or the freezing-point. These results may consequently be employed for diagnostic purposes only when they are extreme, when they extend over long periods of time, and when they cannot be explained by an abnormal diet.

The most pronounced pathologic changes in the molecular concentration of the urine, in the daily osmotic energy of the kidneys, and in the product $Q\,\delta$ are encountered in nephritis, and particularly in the uremia which frequently results. In these cases the retention of urinary solids is very frequently manifested by an abnormally low molecular concentration and a consequent abnormally low daily excretion of molecules. Every improvement of the condition is indicated by an increase of both. According to Strauss, the chronic parenchymatous nephritis cases produce a more marked diminution of the daily excretion of molecules than do the interstitial, since in the latter cases the marked lowering of the freezing-point is more than compensated for by the increased quantity of urine excreted. In diabetes mellitus the osmotic pressure of the urine and the daily excretion of molecules are, of course, greatly increased by the amount of sugar in the urine.

The utilization of cryoscopy in determining the functional activity of a single kidney, the urine from which is obtained either by ureteral catheterization or by Luys' urinary separator, is accompanied by difficulties equally as great as those encountered in studying the mixed twenty-four-hour urine. The object of such examinations is to determine whether one kidney is functionating normally, and whether it will be able to do all the work after the removal of the diseased kidney. The conclusions drawn from the separate cryoscopic examinations of the urines of both kidneys in such cases, which have given rise to a large amount of literature, contain a great many sources of error, only the most important of which will be given. First of all, it by no means follows that the kidney remaining after the extirpation will do the same amount of work as before. Rather, if the diseased kidney still functionated to a certain extent, it is quite possible that the remaining kidney will respond to the increased excretory stimulus and compensate for the defect, even if it apparently did too little work before the extirpation. Upon the other hand, if the function of the healthier kidney be impaired, and yet sufficient to meet the needs of the organism when aided by the diseased kidney, it is possible that it may be insufficient when called upon to do the entire amount of work. These possibilities are not even mentioned in many of the publications upon the subject. Another frequent error is the false supposition that the freezing-point of the urine is the only measure of the functional activity of the kidney. As we have already seen, this is not the case, and the supposition of Kümmel, that a freezing-point of the urine below −1° C. indicates insufficiency of the viscus, is purely arbitrary.[1] Again, in order to reach more accurate conclusions, the quantity of urine excreted must also be considered. This cannot be correctly done, however, since it is not possible to collect the twenty-four-hours' urine from a single kidney. Great caution is also necessary when the results of the cryoscopic examination of the separate urines are employed for the purpose of comparing the functions of the two kidneys.

[1] Such conclusions would be more justifiable if all fluids were interdicted before the examination of the patient, in which case the approximately healthy kidney would always excrete a concentrated urine with a marked lowering of its freezing-point.

This examination is usually made by catheterizing first one and then the other ureter, and then comparing the freezing-points of the two urines. Although the excretion of the urines is approximately simultaneous, it is not exactly so; and, since the excretion of the urine is subject to sudden temporary variations, the comparison is not accurate. Even if the two urines were excreted simultaneously, as is the case when Luys' separator or simultaneous catheterization of the ureters is employed, we should be by no means sure of obtaining comparative values, since experiments upon animals prove that the excretions of the two kidneys are not always alike. It is, therefore, justifiable to assume a difference in function only when repeated examinations always demonstrate similar variations. The fact that, in the customary utilization of the cryoscopic findings, the surgery of the kidney is usually correct, in spite of these errors, may be partly due to the fact that the indication for the operation is not based exclusively upon these results, but also the chemical and microscopic examination of the separate urines.

In view of the objections to the utilization of the cryoscopic findings, we are justified in raising the question as to whether this new method of urinary examination is of more value than a very old procedure dealing with similar questions —namely, the determination of the specific gravity. It is quite clear that the determination of the osmotic pressure or of the freezing-point is not equivalent to the determination of the specific gravity. The determination of the freezing-point furnishes a relative idea of the number of molecules excreted, irrespective of their quality, and the result of such a determination is theoretically independent of the specific gravity of the urine, since molecules of low and high specific gravity exert exactly the same influence upon the freezing-point. The specific gravity, on the contrary, is dependent not only upon the number of molecules dissolved in a given volume of urine, but also upon their chemical composition or weight. With a single exception, presently to be mentioned, this difference, however, is more theoretic than practical. The quality of the excreted molecules in different urines is subject to such slight variation that a marked parallel usually exists between the lowering of the freezing-point and the specific gravity; and if the specific gravity of the urine of a patient rises or falls, we may rest assured that the lowering of the freezing-point of the osmotic pressure has undergone a similar variation. We are consequently just as much justified in drawing conclusions in reference to the work done by the kidney from the specific gravity of the urine as from the height of the osmotic pressure. One exception, however, must be borne in mind: If the urine contain protein, this substance may be responsible for a considerable part of the specific gravity, since it is heavier than water, but it has no perceptible influence upon the osmotic pressure or the freezing-point. Since the protein molecule is very large and heavy, quite a small number of such molecules may cause a rise in the specific gravity without appreciably influencing the freezing-point. With an albuminous urine we should consequently not be justified in attributing a high specific gravity to increased renal activity, particularly since the protein is not secreted by the kidney, but is an indication that the filtering action of the kidney has been impaired by inflammation. With this exception, however, the author maintains that the determination of the specific gravity gives us the same indication of the work done by the kidney as does the determination of the freezing-point. In order to draw similar conclusions from the specific gravity of albuminous urine, it is necessary simply to remove the albumin and then utilize the specific gravity of the remaining fluid. Just as in the estimation of the total work done by the kidneys from the determination of the freezing-point, the urine examined must be a portion of the mixed twenty-four-hours' elimination if correct conclusions are to be obtained. In doing this we may calculate a product whose significance completely corresponds to the significance of the cryoscopic product $Q\,\Delta$ (see above), by multiplying the last two figures of the specific gravity, carried to the third decimal place, by the amount of urine secreted in twenty-four hours. The number so obtained gives a relative idea of the amount of urinary solids secreted in twenty-four hours. We may, however, easily obtain absolute quantities, as stated upon p. 552, by multiplying the last two figures of the specific gravity by 2.23, and then multiplying this product by the daily urinary excretion expressed in liters. The resulting figure is the approximate number of grams of urinary solids excreted in twenty-four hours. The author believes that this number is just as good an indication of renal activity as is the number of molecules excreted daily, provided that any protein present be removed before the specific gravity is determined. The number is, of course, markedly influenced by the quantity of ingested food and water, so that the normal is hard to determine, and the same difficulties are encountered in drawing accurate conclusions as have been previously mentioned in reference to the determination of the

number of excreted molecules. In an entirely analogous manner the specific gravity of the urines (after the removal of protein, if present) obtained by ureteral catheterization or Luys' separator (see p. 558 et seq.) may be utilized in place of the osmotic pressure for the critical study of the urine of each kidney; but, owing to the impossibility of obtaining the total twenty-four-hours' urine, this procedure is open to the same objection previously mentioned in our consideration of osmotic pressure. The author must also take this occasion to claim that cryoscopy has not materially aided our diagnostic ability in reference to the critical study of renal activity, since all the facts learned by ureteral catheterization could also have been discovered by means of the specific gravity. Cryoscopy accidentally became popular and was given preference over the older method from an exaggerated idea of its value, just as all new methods are usually supposed to be an advance over those formerly employed. In addition to the fact that it is not necessary to remove protein, it must nevertheless be admitted that cryoscopy possesses one distinct advantage, particularly in the study of the separate urines, in that it requires a smaller amount of urine than is necessary for the determination of the specific gravity. Nevertheless, the chief advantage of the introduction of the new method has been that it has caused us to study these questions more carefully than was done by means of the specific gravity, since the latter method had not the charm of novelty. We shall subsequently learn that the case is quite different with reference to the cryoscopy of the blood, which is of special significance for general pathology and diagnosis.

How closely the conclusions obtained by means of the determination of the freezing-point of the urine correspond to those which the practical physician may deduce much more readily from the specific gravity is best shown by the statement of G. Fuchs,[1] that in a urine free from protein and sugar the lowering of the freezing-point may be empirically calculated by multiplying the last two figures of the specific gravity, carried to the third decimal place, by 0.075° C.

The far-reaching calculations and conclusions (based upon the freezing-point of the urine) which Koranyi[2] and others have formulated in regard to the freezing-point of the blood, as well as to the amount of sodium chlorid contained in both fluids, will not be discussed, since the author regards their fundamental principles as hypothetic, and in many respects erroneous.

SEDIMENTS AND TURBIDITY OF THE URINE

EXAMINATION OF URINARY SEDIMENTS; SEDIMENTATION; FILTRATION; CENTRIFUGATION; MICROCHEMICAL REACTIONS

Both urinary sediments and turbidity may be frequently enough recognized and characterized, without any microscopic examination, by their physical and chemical behavior. But a microscopic examination is necessary in most cases, especially for the differentiation of organized sediment. If the sediment be very abundant, a drop of the cloudy urine under the microscope will be sufficient; but generally the sediment is so scant that it is advisable to isolate and collect it by sedimentation, filtration, or centrifugation.

In concentrated urines with uratic sediments the microscopic examination of other constituents, and particularly of the organized elements, is frequently rendered very difficult by the presence of urates. In such cases the urates should be dissolved by heating the urine slightly and adding enough water to hold the urates in solution upon cooling. If this cannot be accomplished, which may be the case if uric acid has also been thrown down, both substances may be brought into solution by rendering the urine alkaline by the addition of a solution of soda. A borax solution may also be employed for the same purpose (see below). Such a solution of the precipitated urates and uric acid may be necessary not only for the direct microscopic inspection of the remaining

[1] Zeit. f. angewandte Chemie, 1902, p. 1072.
[2] Zeit. f. klin. Med., 1897.

deposits, but also as a preliminary to sedimentation, filtration, or centrifugation. In certain cases sediment of phosphates or of carbonates may similarly interfere with the microscopic examination. These sediments may be readily dissolved by acidulating the urine with hydrochloric acid.

For Sedimentation.—A tall, pointed glass is filled with the urine, and the sediment is examined under the microscope just as soon as enough has settled to be plainly visible at the bottom of the glass. This usually requires a few hours. The sediment is picked up with a pipet while the upper end is closed with the finger. By slightly decreasing the pressure of the finger a certain amount of sediment is allowed to enter the pipet. It is then closed again, removed, and carefully dried, while the finger pressure is kept constant. A drop of its contents is then allowed to flow upon a glass slide by slightly releasing the finger.

Strassburger has recently recommended diluting the urine with two parts of alcohol, in order to hasten sedimentation by diminishing the specific gravity of the fluid. But alcohol will precipitate proteins, so that this procedure can be recommended only where the amount of these bodies is very slight or where the presence of an amorphous precipitate will not produce confusion, especially for the microscopic demonstration of tubercle bacilli or other bacteria.

The urinary sediment changes so quickly that it is important to examine it as soon after settling as possible.

The various constituents of a sediment differ in their specific gravities; hence, in many cases it is advisable to select specimens for examination at varying depths of a sediment. With practice and care this selection can be made while picking up one specimen.

To prevent bacterial decomposition, so prone to occur during the summer months, it is a good plan to add to the urine one-fifth its volume of chloroform water (1 : 200) or a small piece of camphor, and to select a cool place for the sedimentation. To avoid obscuring the examination of organized sediments by the formation of heavy urate sediments in very concentrated or very acid urines, we may add to the urine one-fifth to one-third its volume of a saturated (1 : 17) borax solution. This solution will not coagulate proteins, and at the same time will act antiseptically. If bacteria alone are sought for, the addition of alcohol mentioned above is to be recommended. If the sediment be very scanty, the filtration method may be employed. As large an amount of the urine as possible is filtered, and the residue upon the filter is picked up with the ordinary pipet while only a few drops of the urine remain.

The centrifuge[1] is now employed in practically all laboratories for obtaining the sediment. With it the sediment may be obtained for examination within a few minutes and from very small specimens of perfectly fresh urine.

Many chemical reactions which reveal the nature of certain sediments can be performed macroscopically and also observed under the microscope. In the latter case, *e. g.*, to determine the nature of unfamiliar crystals, a drop or two of the agent is allowed to run under one edge of the cover-glass, or perhaps sucked under with the help of a piece of filter-paper at the other edge.

[1] Stenbeck, Zeit. f. klin. Med., 1892, vol. xx, 457. Litten, Deut. med. Woch., 1891, p. 23.

The amount of the sediment is best estimated by von Posner's method of estimating the amount of pus present (p. 686). (See p. 681 et seq. in regard to the preservation of organized sediment.)

INORGANIC CRYSTALLINE AND AMORPHOUS SEDIMENTS AND MIXTURES

THE URATES

When the urine cools, urates may settle to the bottom, especially if the sample be concentrated, scanty, or strongly acid, *e. g.*, the urine of congestion and of fever, less often the urine of nephritis. The sediment will then present a fairly characteristic appearance, clay-colored, reddish yellow, brick red, or rose red (sedimentum lateritium). Sometimes it adheres to the wall of the urine glass as a thin coating. Unlike all other sediments, it dissolves extremely readily even with very gentle heating, and so can be accurately recognized. The addition of acid will also dissolve urate sediments with a gradual separation of uric-acid crystals. The addition of alkalis also dissolves the precipitate particularly easily, and often with the separation of phosphates. The ordinary urate sediments consist of a mixture of sodium, potassium, calcium, magnesium, and ammonium urates. Sodium urate predominates. With the exception of ammonium urates, the urates appear only in acid urine. They are formed by a double rearrangement between acid sodium phosphate and the neutral urates held in solution, from which acid urates are formed, which are not very soluble and become precipitated. Aside from these chemical processes, the cooling of the urine favors the separation of urates. That the mere cooling of the urine alone will not, however, produce the separation is shown by the fact that the sediment forms sometimes only a considerable time after the cooling, and also by the fact that a urate sediment usually does not entirely dissolve until the urine is heated to a temperature above that of the body.

Urate sediments often contain crystals of pure uric acid, which also arise from the double rearrangement mentioned above.

The peculiar pronounced brick- or rose-red color of some urate sediments arise from uroerythrin, a pigment as yet little understood. (Compare p. 582.) It seems to be formed to excess in certain febrile affections (acute rheumatism, pneumonia).

If a urine with a urate sediment is decomposed by ammoniacal fermentation, the sediment will be partly changed to acid ammonium urate. The latter is the only urate sediment which occurs in alkaline urine. (Compare p. 675.)

Under the microscope urate sediment appears as fine amorphous granules. If acetic acid be added, characteristic crystals of uric acid may be seen to shoot out from these granules (Fig. 253). Ammonium urate presents characteristically shaped crystals (Fig. 256, *b*). It occupies an exceptional position in occurring in alkaline urines together with phosphates and carbonates, and not as do ordinary urates. If a urine containing ordinary urates has been rendered alkaline by fermentation, one may find a mixture of alkaline and ammonium urates before the urine has actually become alkaline. Uratic sediments respond to the murexid test. (See p. 672, under Uric Acid.)

As already mentioned, the concentration of the urine and its acidity are particularly important in the formation of urate sediments. Urates

(with the exception of ammonium urate) are deposited more rapidly with increasing acidity of the urine. If, therefore, despite a normal specific gravity, a urine very readily deposits a sediment of amorphous urates, it does not signify, as was formerly supposed, an increased production of uric acid, but usually merely an increase in the acidity of the urine—*i. e.*, an increased amount of the acid sodium phosphates. There is, however, no doubt that the formation of urate deposit is often dependent on an increased excretion of uric acid, for example, in leukemia and after inflammatory processes (perityphlitis, pneumonia), where the resorption of the products of the breaking down of leukocytes leads to increased uric-acid excretion.

URIC ACID IN THE SEDIMENT

Crystals of uric acid occur in the urine at the same time with amorphous urate sediments, and sometimes without any separation of urates, mostly as a fine crystalline precipitate, often adherent to the walls of the

Fig. 253.—The more common forms of uric-acid crystals (after Bizzozero, Scheube, and Späth).

vessels (Fig. 253). The beautifully shaped, sparkling, shining crystals of red-brown color can often be recognized by the naked eye. Their appearance is usually very characteristic. The variety of forms under

which uric acid crystallizes is almost without number. Hence, a brown-colored crystal always suggests uric acid. Uric acid may also be precipitated as colorless crystals. Both uric acid and urates reduce alkaline solutions of copper (Trommer's test). In case of doubt the *murexid* test may be performed with a few small crystals. The latter are heated with dilute nitric acid upon a porcelain plate or dish. Solution takes place with effervescence. After evaporation there remains a reddish residue, which turns a beautiful purple red upon the addition of a little diluted ammonia, due to the formation of ammonium purpurate (murexid). The addition of potassium hydroxid will change the color to violet. The urates also react to the murexid test.

Guanin, xanthin, and epixanthin, which give somewhat similar reactions to uric acid (see Xanthin, p. 678), do not occur as sediments in the urine, and are differentiated by their solubility in hydrochloric acid.

The most frequent shapes which the uric-acid crystals present under the microscope are depicted in Fig. 253.

If uric-acid crystals are observed in the sediment at the same time as amorphous urates, they have the same significance as the latter. They may be found in any concentrated urine. Rapid precipitation of purely crystalline uric acid without any amorphous urate in a comparatively abundant urine shows that it is strongly acid. Such a condition has nothing to do with the so-called uric-acid diathesis (gout and uric-acid calculus). Moritz has demonstrated that every individual crystal of uric acid has an albuminous ground-substance.

CALCIUM OXALATE IN THE SEDIMENT

These crystals occur both in pathologic and in normal urine. The sediment is usually scant, and recognized only when examined microscopically. An abundant oxalate sediment is often noticed after the ingestion of food-stuffs rich in oxalic acid (fruit, especially tomatoes, etc.). The appearance of oxalate crystals in the urine independent of a diet containing the salt of the acid has been termed oxaluria, and writers have indicated it as a special metabolic anomaly of the same general type as diabetes mellitus and gout. It must be pointed out that the condition is not always one of increased oxalate excretion, but may be that of a condition favorable to the precipitation of the crystal. Cases have, however, been examined where the analysis showed an increased excretion of oxalic acid, and this was the cause of the oxalate sediment. These cases may properly be called oxaluria. There is, as yet, no reason for looking upon them as a distinct anomaly of metabolism. Oswald[1] believes that increased oxalic acid excretion is associated with those diseases in which there is an increased breaking down of tissue, and that the source of the oxalic acid is the connective tissue. This coincides

Fig. 254.—Crystals of calcium oxalate: *a*, So-called envelopes; *b* and *c*, rarer forms (after Scheube).

[1] Oswald, Lehrb. der chem. Pathologie, Veit, Leipzig, 1907.

with the observation that one obtains an increased excretion not only in diabetes mellitus and gout, but in typhoid, pulmonary tuberculosis, and pernicious anemia.

The formation of oxalate calculi will, of course, be favored by such a condition. According to Fürbringer, calcium oxalate is in all probability a normal urinary constituent, held in solution in the urine by the acid sodium phosphate. If for any reason the acid reaction is reduced so that the acid phosphate becomes converted to a neutral salt, calcium oxalate becomes precipitated. Ordinarily, the double change between neutral urate and acid phosphate mentioned in connection with the urate sediments is the cause of the reduction of the acid reaction; and then, besides the urates, calcium oxalate precipitates. The separation of the oxalate usually takes place very slowly, and it therefore generally occurs as well-formed crystals (Fig. 254). They usually present a very characteristic octahedral type (envelope); but other varieties also occur (see Fig. 254, note to Fig. 255), which cannot, however, be recognized immediately from their shape.

From the way in which calcium oxalate crystals separate, it is plain that they may occur in faintly acid, in neutral, and in faintly alkaline urine. Calcium oxalate crystals are characterized not only by their shape and insolubility in acetic acid, but by the fact that they are soluble in hydrochloric acid.

A tendency to the formation of oxalate calculi will be found in those cases where oxalate sediments occur in the urine.

The foregoing explanation of the separation of calcium oxalate crystals makes it evident that their appearance in the sediment does not justify the assumption of increased formation of oxalic acid any more than urate sediment necessarily implies increased uric acid. "Oxaluria" is often diagnosed without sufficient reasons. An increase of the oxalic acid elimination can be determined only by a quantitative urinalysis.

SEDIMENTS OF THE EARTHY PHOSPHATES AND CARBONATES AND OF AMMONIUM URATE

They are usually light in color, because they are less inclined than the urates to absorb the urinary pigments, and because their separation does not depend so much upon the degree of concentration as upon the reaction of the urine.

1. **Amorphous Earthy Phosphates and Carbonates.**—Normal and basic phosphates and carbonate of calcium and magnesium occur as granular and amorphous masses, and may be present in every alkaline urine, particularly if the alkalinity be due to a fixed alkali. These salts are also precipitated if the urine be artificially rendered alkaline, or if a faintly acid, neutral, or faintly alkaline urine be boiled, the acid combinations in which calcium and magnesium phosphate and carbonate are dissolved in the urine being changed to basic combinations by boiling. Their precipitation produces a turbidity which, unlike the precipitate of protein from heating, is soluble in dilute acids. The carbonates when dissolved by dilute acids give off CO_2, a peculiarity which will distinguish them from the phosphates.

A crystalline precipitate of calcium carbonate sometimes appears as a sandy powder mixed with the amorphous phosphate sediments. Microscopically, it consists of spheric or dumb-bell-shaped formations (Fig.

255), which dissolve in acetic acid with the evolution of gas, and so can be distinguished from similar formations of calcium oxalate. (See p. 673.)

2. **Ammoniomagnesium Phosphate (Triple Phosphate) and Ammonium Urate.** — These are combined with the amorphous phosphate and carbonate sediment if the alkaline reaction of the urine be entirely or partially due to the formation of ammonium carbonate within

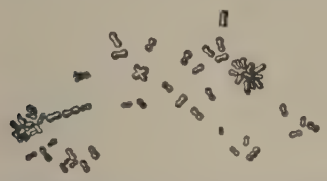


Fig. 255.—Indistinct crystalline sediment (dumb-bell crystals) of calcium carbonate. Similar crystals are formed by calcium oxalate and calcium sulphate (after Funke).

Fig. 256.—*a*, Crystals of ammoniomagnesium phosphate (triple phosphate); *b*, crystals of ammonium urate (after Neubauer and Vogel).

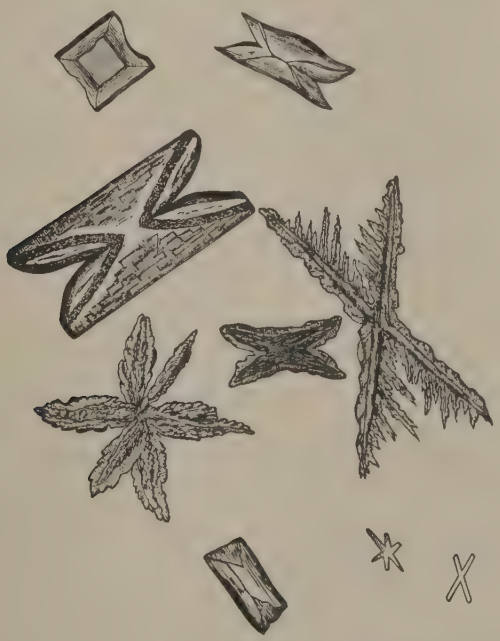


Fig. 257.—Other forms of triple phosphate crystals (after Peyer).

the urinary passages from the urea, or, after voiding the urine, from bacterial fermentation. In such a condition triple phosphate will compose

the major part of the sediment. The large, characteristically shaped prisms, the so-called "coffin-lids" (Fig. 256, *a*), are readily recognized under the microscope. The ammonium urate which so frequently accompanies the triple phosphate crystals (Fig. 256, *b*) is the only urate precipitated in an alkaline urine. This salt forms dark-colored spheres with projecting spines, "star or thorn-apple balls." Crystals of ammonium urate dissolve in acetic acid with a gradual formation of uric acid. Ammoniomagnesium phosphate crystals are also readily soluble in acetic acid. Although both these crystalline forms occur chiefly in ammoniacal urine, they also appear in faintly acid or amphoteric urine if an ammoniacal fermentation has commenced.

3. **Dicalcium phosphate** (neutral or simple acid calcium phosphate) is a rather rare sediment, formed in faintly acid or amphoteric urine as microscopic prismatic or wedge-shaped prisms grouped as rosets (Fig. 258). These crystals are soluble in acetic acid. The rosets are frequently only indistinctly developed.

4. **Crystalline Trimagnesium Phosphate.**—In very rare cases there have been observed in alkaline urine large, flat, strongly refractive masses which consist of elongated rhombic plates with angles of 60° and 120°. These are trimagnesium phosphate (normal magnesium phosphate).

THE SO-CALLED PHOSPHATURIA

The occurrence of phosphate sediments in the urine has been termed phosphaturia, and a latent condition, in which the phosphates are separated out on boiling has been differentiated from that in which the urine is voided in a turbid state. The sediment is mostly amorphous phosphates, sometimes accompanied by carbonates. The term phosphaturia may be used, but was not altogether understood by the older writers, who assumed that it was an anomaly of metabolism, associated with an increased output of phosphates or phosphoric acid. It may be demonstrated that the excretion of a phosphate sediment, either before or after boiling the urine, is always associated with a decreased acidity of the urine, or the urine may sometimes be actually alkaline. A phosphaturia, with the precipitation of phosphates and carbonates, is most often observed when, through vomiting or lavage, a portion of the hydrochloric acid secreted by the stomach is not absorbed in the intestine, and so is definitely lost to the body. Other cases are seen where the urine of healthy individuals is excreted turbid, especially after meals (mostly, however, of the latent type), and a permanent condition of this kind is seen in gastric hyperacidity. The temporary excretion of phosphates after meals is explained by assuming that during the time of digestion the blood and urine become more alkaline than normal, owing to the secretion of hydrochloric acid into the stomach. The permanent conditions are to be explained by assuming that, owing to the hyperacid condition of the stomach, the acid is not absorbed and the alkali balance of the body increases. Naturally, other causes, which have been mentioned in connection with the decreased acidity of the urine (see p. 556), favor the precipitation of phosphates. In those cases where the urine has undergone alkaline fermentation, triple phosphate crystals will be found. The phosphaturia which is found in neurasthenic patients is a somewhat special condition. Some of these cases void a turbid urine continually under conditions which are independent of meals. The phosphaturia may be latent. It was previously believed that this was a special disturbance of metabolism—a so-called phosphatic diathesis. It has been shown that these cases do not have an increased excretion of phosphoric acid, which was supposed to have its origin in increased catabolism of nervous tissue. The excretion of calcium is increased. It would, therefore, appear that, in the increased excretion of calcium as a base, the urine decreases in acidity or even becomes alkaline. Soetbeer and Krieger[1] found in these cases, instead of a normal daily excretion of about 0.2 gm. calcium, the amount rose to 0.7 gm., and the ratio of calcium to phosphoric acid changed from 1: 12 to 1: 1.5–2. An explanation of this puzzling form, which should rightly be called a calcaruria, has not been given. It is uncertain whether it is an anomaly of the mineral metabolism

[1] Deut. Arch. f. klin. Med., 1902, lxxii, 553.

(not of phosphoric acid, but of calcium), or whether it is due to a functional disturbance of the kidney; further, whether the nervous condition is a cause or a sequel, or whether they are both symptoms of a more deeply seated condition. As there are no signs of a destruction of calcareous tissue, one must assume that the intestine, which excretes the greater part of the calcium, fails in its function and more calcium than normal is absorbed.

Clinically, in all forms of phosphaturia, in consequence of the decreased acidity of the urine, the dissociation of the ammonium salts is increased, and ammonia may be detected by placing a strip of moistened red litmus-paper above the urine without there being alkaline fermentation or increased excretion of ammonia.

It may be pointed out that it is often difficult to make out a decreased acidity of the urine as a common cause of phosphaturia. The precipitated phosphates are neutral or basic salts and take out basic substances from the urine, so that the clear fluid may show no decrease in acidity. In order to demonstrate such a masked decreased acidity, it is necessary to bring the phosphates into solution by the addition of a known volume of normal hydrochloric acid, and perform the titration, subsequently subtracting the acidity due to the amount of acid added.

The author also mentions that traces of albumin often accompany a phosphaturia. The significance of this has not been made out. (See Phosphatic Albuminuria, p. 562.)

Incompletely differentiated from the above are the symptom-complexes described by Tessier as phosphatic diabetes[1] and the "phosphaturie terreuse des dyspeptiques" of A. Robin.[2]

OTHER INORGANIC SEDIMENTS OR TURBIDITIES (RARE)

Gypsum (calcium sulphate) occurs very rarely, and only in the sediment of strongly acid urine. Its crystals are represented in Fig. 259. (Compare Fig. 255.) They are insoluble in ammonia, alcohol, and acetic acid; slightly soluble in hydrochloric acid, nitric acid, and hot water. Their aqueous solutions may be precipitated

Fig. 258.—Crystals of dicalcium phosphate from amphoteric urine (alter Neubauer-Vogel and Ultzmann-Hofmann).

with barium chlorid, and the resulting precipitate is insoluble in hydrochloric or nitric acid. Ammonium oxalate also removes them from their aqueous solutions, and the resulting precipitate is insoluble in acetic acid, but soluble in nitric and hydrochloric acids.

Cystin.—Cystin occurs in the urine only very rarely (so-called cystinuria).[3] This is a peculiar metabolic anomaly which leads to the formation of cystin and diamins. It was thought to be due to some peculiar intestinal mycosis, because these substances are also found in the intestinal contents. More recent investigations have shown that it is probably caused by an incomplete catabolism of the protein

[1] Lyon Med., 1875, xix, 307. [2] Bull. gén. d. therap., 1900.

[3] See Stadthagen and Brieger, Berlin. klin. Woch., 1889, vol. xxvi, p. 344, and Udránsky and Baumann, Zeit. f. physiol. Chem., 1890. The more recent literature will be found in an article by Blum, Semaine médicale, 1906, No. 47.

molecule. According to this view, both cystin and the diamins are normal products of intermediary protein metabolism, and their excretion in the urine is due to a failure on the part of the liver to catabolize them further. Cystin usually separates from an acid urine within the urinary passages in characteristic hexagonal, plate-like, colorless crystals (Fig. 260) (cause of cystin calculi).

Uric acid also separates in similar crystals, although quite exceptionally; hence cystin and uric acid may be confounded. The crystals of cystin are, however, perfectly colorless. To differentiate doubtful crystals chemically, ammonium

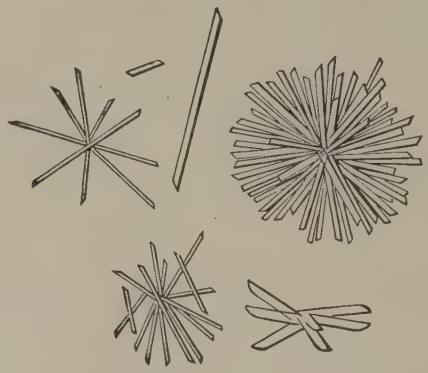


Fig. 259.—Crystals of gypsum (after Neubauer and Vogel).

hydroxid is added to the sediment. Cystin will be dissolved. The filtrate is then acidulated with acetic acid or, better still (Salkowski, Drechsel), allowed to stand exposed to the air for some time until the ammonia has escaped. Cystin will then be again precipitated in hexagonal disks. Uric acid is only very slightly soluble in ammonia, and also differs from cystin in being only slightly soluble in hydrochloric acid.

Tyrosin and Leucin.—Tyrosin very rarely appears as a sediment. It is recognized by its characteristic crystals. (Compare p. 605 and Fig. 240.)

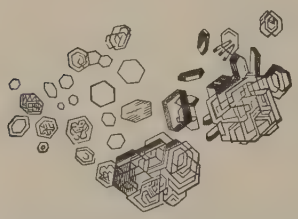


Fig. 260.—Crystals of cystin (after Neubauer and Vogel).

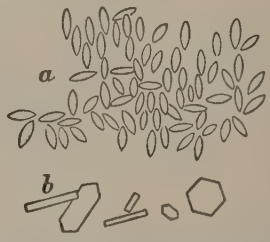


Fig. 261.—*a*, Xanthin crystals; *b*, crystals from the solution of xanthin in hydrochloric acid (after Neubauer and Vogel).

Leucin is a still rarer sediment than tyrosin, and is then always associated with the latter. (Compare p. 605.)

Xanthin, although a normal urinary constituent, is very rarely observed as a sediment, and then under entirely unknown conditions. It forms whetstone-shaped crystals, which are differentiated from those of uric acid by being readily soluble in ammonia. Further, if xanthin crystals are evaporated with moderately concentrated nitric acid over a water-bath, they leave a yellowish-white residue, which turns to an intense yellow after careful heating over a small flame; then the addition of potassium hydroxid will change the color to a yellowish red, which

will become more deeply colored when freshly heated, and which will finally turn to a violet red when the potassium hydroxid is evaporated (Strecker). This test must not be confused with the murexid reaction (p. 673).

Cholesterin.—Cholesterin crystals have been found occasionally, and sometimes in considerable quantity (cholesterinuria), in the urine in diseases of the urinary passages (inflammation of the bladder, pyelitis, echinococci, chyluria, and nephritis). This occurrence is, however, extremely rare.[1] Cholesterin is supposed to be derived from the epithelium (Fig. 278, *b*).

Hematoidin Crystals (*Bilirubin*, compare Fig. 278, d^2).—Hematoidin crystals occur, although very rarely, in the urine of hemorrhagic nephritis. Bilirubin crystals, on the contrary, are not infrequently precipitated in sediment of markedly icteric urine when cool, particularly if it be strongly acid or artificially acidulated. They can be easily recognized by their yellowish-red color, by their solubility in alkalis and chloroform, and by their reaction to Gmelin's test (p. 575 et seq.), under the microscope.

Indigo.—If the indican be increased in the urine, indigo may separate as pointed or rhombic crystals. These may either be found in the sediment or form a scum on the surface. They dissolve readily with a blue color in chloroform (pp. 554 and 579).

Melanin.—Melanin separates in rare cases as fine amorphous granules. It usually remains, however, in solution (p. 582).

Hemoglobin.—This may be precipitated while hemoglobin is still in solution, as a sediment of amorphous cakes or cylinders in hemoglobinuria. (Compare pp. 554 and 572.)

Fat.—A large amount of fat in the urine almost always signifies *chyluria* (lipuria). The urine is then albuminous, of a milk-white to a cloudy-yellow appearance, sometimes even slightly blood-tinged, neutral or faintly acid, forms a cream-like layer, and often contains small coagula. The latter may form within the body as well as after the urine is voided. (Fibrin and Fibrinogen Contained in the Urine, see p. 568.) A microscopic examination shows that the fat is subdivided much more finely in the urine than in the milk. No distinct fat-drops can be seen, but extremely finely divided, almost invisible, fat-granules. These granules furnish the cloudiness and the cream-like layers. The other characteristics of this fatty admixture are the same as those that will be described later on. (See p. 911 in reference to the chylous fluids sometimes found in the serous cavities.) Chylous urine does not contain sugar, since this substance is not removed from the intestine by the lacteals, but by the veins. Chyluria is well known to be a tropic disease caused by a thread-worm, Filaria sanguinis, which inhabits the blood. The urine occasionally contains the embryos of the filariæ. (See Fig. 272.)

The occurrence of tropic chyluria is due to the presence of adult filariæ in the thoracic duct, producing a stasis of the chyle, which extends not only to the lymphatics of the intestines, but also to those of the urinary apparatus. In such cases chyle may become admixed with the urine by diapedesis or by rupture of those lymphatics which do not ordinarily contain chyle. In one case Havelburg succeeded in definitely proving that the escape of chyle into the urine took place in the bladder. The frequent simultaneous admixture of blood is to be explained, according to Scheube, partly by the coincident rupture of blood-vessels and varicose lymphatics, and partly by the disappearance of the tissue between the venous and lymphatic vessels, due to the lymph stasis, whereby the contents of the lymphatics become mixed with blood. A similar stasis of chyle, produced in different ways in individual cases, may probably be the cause of the rare chyluria observed in this climate. These cases may be explained by the observation of Porf,[3] which, by reason of pressure from a tuberculous gland on the thoracic duct, caused the appearance of chyle in the pelves of both kidneys, due to the stasis of the fluid.

If the amount of fat contained in the blood be abnormal (lipemia), the urine also contains an abnormal amount (bone fractures, fat-embolism, diabetes mellitus, alcoholism, and acute phosphorus-poisoning). (See Examination of the Blood.)

A small amount of fat is also found in the urine in Bright's disease when the kidney elements (casts and epithelium) are eliminated in a fatty degenerated condition. The fat is then ordinarily inclosed within cells or casts, but exceptionally it may appear as fat-drops floating upon the surface, as a result of the degeneration of the cells or casts. Crystalline needles of fat have in a few cases been

[1] Cf. Hirschlaff, Deut. Arch. f. klin. Med., vol. lxii, p. 531.
[2] Hematoidin and bilirubin are usually considered identical.
[3] Zeit. f. klin. Med., 1906, lix, pp. 2–4.

found in the urine. Such crystals are sometimes formed within the body, sometimes only outside from the fluid fat (Fig. 278, *a*).

The examiner must, of course, be careful not to confound contamination from dirty vessels or catheter grease with *lipuria*.

If the macroscopic or microscopic appearance of the urine does not suffice for the demonstration of fat, then the urine should be extracted with ether. After evaporating the ether the physical characteristics of the fat are more easily recognized (grease spots), or an odor of acrolein (like smoking tallow candles) can be demonstrated if the residue be heated on a platinum foil, or, if the fat contain oleic acid, the addition of a 1 per cent. solution of osmic acid will turn the residue black.

According to Späth, *hippuric acid* has been observed in urine, in rare cases in the shape of prisms or needles. The factors governing its occurrence are not yet definitely known, although it seems to have been more frequently observed after the administration of salicylic acid.

MUCOUS SEDIMENTS

If the urine contain considerable nucleo-albumin (compare p. 571 et seq.), it will separate spontaneously as a sediment of mucus-like consistence. Such a sediment consists microscopically of a cloud of clotted, transparent, indistinct masses. The addition of acetic acid will make their contours more distinct. They sometimes inclose various morphologic elements, white blood-corpuscles, epithelium, crystals, etc. Epithelial elements and white blood-corpuscles are almost always found in mucous sediments, because the increased nucleo-albumin is the product of a catarrhal disintegration of the mucous membrane.

ANALYTIC SCHEME OF THE PRINCIPAL INORGANIC URINE SEDIMENTS

Readily soluble upon heating: Urates.

Insoluble or soluble only with difficulty upon heating.

- Soluble in acetic acid:
  - Phosphates, no effervescence.
  - Calcium carbonate with development of carbonic acid.
  - Ammonium urate with microscopic precipitation of uric acid.
- Insoluble in acetic acid:
  - Calcium oxalate.
  - Leucin, tyrosin, xanthin, cystin. — Soluble in hydrochloric acid, the last four soluble in ammonia.
  - Uric acid.
  - Gypsum. — Insoluble in hydrochloric acid.

APPENDIX TO DISCUSSION OF INORGANIC SEDIMENTS. URINARY CALCULI

Many of the substances enumerated as inorganic sediments are, under certain conditions, eliminated in the urine in the shape of concretions or urinary calculi.

Only the most important points in recognizing the various forms of urinary calculi will be mentioned here. The earthy phosphatic calculi are distinguished by their friability. The commonest calculi, those of uric acid and urates (urate calculi), are far more firm. The hardest of all are the calculi of calcium oxalate (so-called oxalate calculi).

The rare cystin calculi are usually yellow, smooth, small, and soft as wax; the still rarer xanthin calculi are clearer, rather hard, and when rubbed, exhibit a wax-like polish. Calculi of cholesterin are also very rare and resemble the cystin concretions. The concrements, consisting of fat and of fatty soaps of the alkaline earths and designated as urostealiths, are extremely rare; they are characterized by their light color, soft consistence, and hardness when dried. Mention should also be made of a single recorded instance of a calculus consisting of indigo, which was sufficiently characterized by its color. Urinary calculi frequently consist of different substances arranged in layers, each of which may be more or less distinctly recognized by the previously mentioned characteristics.

For qualitative analysis a finely powdered specimen of the stone is first heated upon platinum foil. If the specimen burns up entirely or nearly so, it is composed of uric acid, xanthin, or cystin. Cystin and xanthin dissolve in dilute hydrochloric acid; uric acid does not. Uric acid may also be recognized by the *murexid test* (p. 673). Xanthin can be distinguished from cystin, as shown on p. 678. To identify cystin, Salkowski digests the powder with ammonium hydroxid, filtered, and evaporates the filtrate in a watch-glass. Cystin crystallizes out in its characteristic hexagonal plates (Fig. 260). Cholesterin is characterized by its solubility in ether and by the beautiful rhombic plates which are formed by evaporating this ethereal solution.

If the powdered calculus does not burn up entirely upon the platinum foil, it must contain either lime or magnesia. If in such a case the powdered specimen completely dissolves in dilute hydrochloric acid, it contains no uric acid along with the alkaline earths. What dissolves must consist of phosphates, carbonates, or calcium oxalate. Carbonates can be recognized by the development of gas. Calcium oxalate can be recognized by the fact that (by acetic acid) it is precipitated gradually, as a flaky cloudiness, from the dilute HCl solution neutralized with clear ammonium hydroxid. If any residue remain after the treatment with dilute hydrochloric acid, it generally consists of uric acid, which can easily be identified by means of the murexid test (p. 673).

ORGANIC ADMIXTURES AND SEDIMENTS OF URINE

As to the method of isolating these, see p. 669 et seq., at which place will be found the necessary information in reference to the elimination of interfering sediments composed of urates, phosphates, or carbonates.

MACROSCOPIC IDENTIFICATION OF ORGANIZED URINARY SEDIMENTS

These sediments differ from non-organized in their insolubility on heating, or even after the addition of hydrochloric and acetic acids. They do not sediment as rapidly as the non-organized, so that a urine from a catarrh of the bladder, or one containing blood, may remain clouded for hours, while a urine containing urates or phosphates sediments rapidly. This is due to the low specific gravity of the former elements. Blood-corpuscles sediment most rapidly; bacteria often not at all. Further distinctions are given in Doune's test for pus, the detection of blood-coloring matters, the behavior of bacteria toward chemic reagents.

PRESERVATION OF THE ORGANIC SEDIMENT

If it be impossible to examine an organic sediment immediately after settling or after centrifuging, it may be preserved by washing several times with a normal salt solution and then kept in 1 per cent. osmic acid. The fat-drops of the cellular elements will be colored black if they contain any oleic acid. Instead of this procedure[1] the sediment, which has been washed with physiologic salt solution, may be hardened in a 1 : 20 sublimate solution for five minutes and then preserved in a 2 to 10 per cent. formalin solution. Formalin will destroy the red blood-corpuscles if they have not been previously hardened in the sublimate solution, hence the hardening by sublimate may be omitted if there are no red cells. May[2] calls attention to the fact that even in a case of this sort the urinary sediment must be first washed, otherwise considerable sediment of spheric crystals of diformaldehydurea readily forms.

STAINING OF THE ORGANIC SEDIMENT

There is no perfectly satisfactory method for staining a urine sediment. Most pigments produce precipitates after being added to the urine, so that the sediment is disfigured by granular masses. Dry specimens are unsatisfactory, because urine with an organic sediment is always more or less albuminous, and dried protein stains strongly; hence the dry preparations are never neat. These disadvantages may be partially obviated, although in a rather cumbersome way, by washing the sediment repeatedly with normal salt solution, repeating the sedimentation, then drawing off the fluid repeatedly with a pipet, thus separating it from the urinary constituents which are held in solution, especially from albumin, and then finally

[1] Gumprecht, Centralbl. f. inn. Med., 1896, No. 30.
[2] Arch. f. klin. Med., vol. lxviii, p. 425.

adding the staining pigment. A cover-glass preparation may then be made in the same manner as with sputum. (See pp. 710 and 715.) The sediment must not be washed for too long a time, however, or sufficient material will not be obtained for the cover-glass. The same rules apply to the staining of the dry preparation as obtain in the examination of the sputum. If the attempt to make a dry preparation be unsuccessful, the moist sediment may be best stained according to the method of T. Liebmann.[1] The urine is centrifuged, the supernatant fluid poured off, and the sediment treated with 2 to 4 drops of a solution of 2 gm. of methylene-blue (Merck) in 100 cc. of a 10 per cent. solution of formalin. The sediment and the staining solution are then well shaken in the centrifuge tube and allowed to stand for several minutes. The tube is then filled with water to remove the salts and the excess of stain, the solution is again centrifuged, and the sediment placed beneath the microscope. Hyaline casts are stained light-blue, waxy casts dark blue, nuclei and bacteria dark blue, and red blood-corpuscles grayish blue. This method may also be employed for specimens preserved with formol.

If it be desired to demonstrate the fatty elements, a good method of staining the urinary sediment is that of Cohn:[2] The dry slide is hardened in a 10 per cent. solution of formalin for about ten minutes, then washed with water, and placed for ten minutes in a concentrated solution of Sudan stain in 70 per cent. alcohol.[3] Fat is stained red and the nuclei violet.

May[4] suggests, in order to prevent the formation of insoluble deformaldehydurea, to wash the sediment before treating it with formaldehyd.

Posner recommends hardening the dry preparation with osmic acid. He proceeds as follows:[5] Several crystals of osmic acid are placed in a wide-mouthed dark-glass bottle provided with an accurately ground-glass stopper. The moist, smeared glass-cover is now placed over the mouth of the open bottle, with the smeared side down. This is accomplished by making the clean side of the cover-glass adhere to a slide by means of a drop of water. The slide is then held in position by the dark-colored stopper, so that light is excluded. Fixation is completed in forty seconds. The cover-glass is then dried in the air, and stained without previous washing. Posner found that this treatment adapted the preparation for all the finer staining methods, and that it was also applicable for blood-preparations.

N. Iagić recommends the method which is given in the section on Puncture, and which is used for staining the cellular elements of an exudate. This method is successful in staining urinary sediments.

EPITHELIUM

Scattered epithelial cells may be found even in normal urine. The desquamation of epithelium is a normal physiologic process. If they are present in large numbers, however, they point to inflammatory and destructive changes of the urinary apparatus. The following kinds may be distinguished:

Renal Epithelium.—They are generally spheric or cubic, a little larger than white blood-corpuscles, often distinguishable from the latter only by their larger size and by their large single nucleus. The nucleus is readily seen, and looks like a bubble, especially when stained. (Compare p. 685.) They may show any degree of fatty degeneration, and may eventually become disintegrated to form a conglomeration of fat-drops. These cells are very uncommon in normal urine, but in some forms of nephritis are very plentiful (Fig. 262).

Epithelium of the Urinary Tract.—These present extremely varied forms. The cells of the upper layers are generally flat, round,

[1] Münch. med. Woch., 1904, vol. xlix, p. 1768.

[2] Zeit. f. klin. Med., 1899, vol. xxxviii, parts 1, 2, and 3. This article also contains good illustrations of urinary sediment stained by this method.

[3] The solution is prepared by Dr. Grübler, Leipzig, Bayrische Strasse 63. Hematoxylin is used as a counterstain, and the specimen mounted in glycerin.

[4] Arch. f. klin. Med., lxviii, 425.

[5] Berlin. klin. Woch., 1903, vol. xxxii.

or polygonal; those of the deeper layers are elongated and provided with processes. Fig. 263 illustrates a number of these cells. A considerable quantity of the epithelium of the urinary passages is thrown off in all inflammatory processes. It was formerly believed that all cells provided with prolongations always came from the pelvis of the kidney. Unfortunately for the differential diagnosis of pyelitis and cystitis, this old idea is not true. No absolute point of differentiation between epithelium of the pelvis of the kidney and that of the bladder has yet been found. Nevertheless, a very great predominance of caudate epithelium, as compared with the permanent variety, suggests pyelitis rather than cystitis. Fig. 264 represents the sediment taken directly from the pelvis of the kidney in a case of pyelitis.

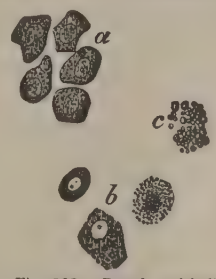


Fig. 262.—Renal epithelium from nephritic urine: *a*, Polyhedral renal epithelium in nephritis of scarlet fever; *b* and *c*, different grades of fatty degeneration in renal epithelium in chronic nephritis (× 400) (after Bizzozero).

Vaginal and **preputial epithelia** are typical large pavement cells. Their shape should be familiar, because their accidental occurrence in the urinary sediment may lead to the erroneous presumption of desquamative affections of the urinary tract. If a catheterized specimen be examined, no such mistake is possible.

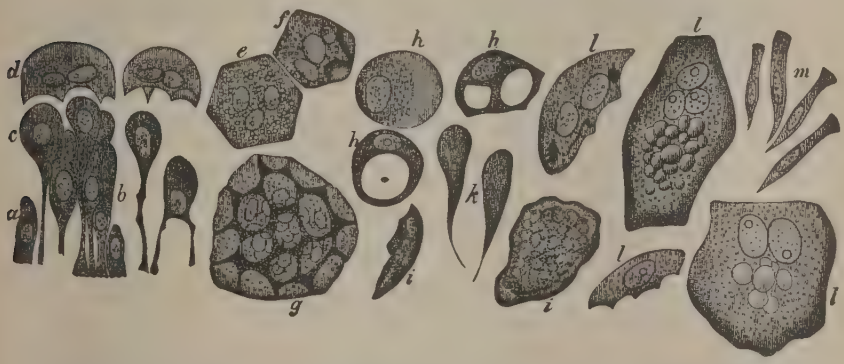


Fig. 263.—Epithelium of urinary passages: *a*, *b*, *c*, *d*, Profile of cells in their normal position: *a*, cell of deep layer; *b*, long cell of second layer; *c*, simple- and double-caudate cells; *d*, flat surface cell; *e*, surface appearance of superficial flat cell with three nuclei; *f*, surface appearance of superficial flat cell with one nucleus and four impressions (Nischen); *g*, surface appearance of superficial flat cell with many nuclei and many impressions; *h*, *i*, *k*, epithelium of bladder modified by action of urine; *h*, from alkaline urine, one cell swollen, the other two with vacuoles; *i*, surface cells; *k*, caudate cells; *l*, bladder epithelium, granular and stained yellow by blood-pigment, from a case of cystitis and nephritis; *m*, cylindric epithelium of male urethra (× 370 to 400) (after Bizzozero).

PUS-CELLS

Pus-cells may also appear in the urine in all inflammatory processes of the urinary tract or kidneys or when an abscess breaks into the urinary tract. Their number may vary greatly. Sometimes they form the chief part of an abundant sediment, and sometimes they are only

found scattered. When the urinary tract is diseased, the amount of pus in the urine may be great, but in disease of the renal parenchyma proper, the pus-cells are usually very few. The origin of the pus-cells can be determined with some degree of certainty only when the presence of other morphologic elements (epithelium, casts) serves as an indicator.

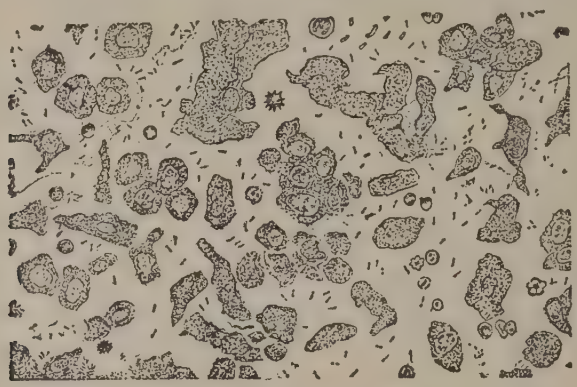


Fig. 264.—Sediment from a case of pyelitis, taken directly from the pelvis of the kidney at the post-mortem examination.

The sudden appearance of a pus sediment in the urine suggests the rupture of an abscess into the urinary tract, provided that the other clinical signs correspond with this assumption. The occurrence of thread-like formations is very characteristic of a gonorrheal sediment (gonorrheal

Fig. 265.—Sediment in alkaline inflammation of the bladder: pus, epithelium, and triple phosphate crystals (after Peyer).

threads, compare p. 690). They consist of pus-cells glued together with mucus.

In females the pus sediment may come from the vagina. To exclude such a possibility, either the vagina must be thoroughly irrigated before the urine is voided, or the urine must be drawn with a catheter.

With alkaline fermentation a pus sediment is oftentimes converted into a ropy, gelatinous mass by the swelling of the pus-corpuscles. Purulent urinary sediments are often of a slimy consistence, even if the urine be not alkaline, because the urine in inflammatory affections usually contains nucleo-albumin.

The pus-corpuscles voided in the urine vary in their microscopic appearance, which depends partly upon the length of time since their escape from the blood-current, and partly upon the consistence of the urine, or upon the nature of the affection in question. Sometimes they are very cloudy and shrunken, so that the nuclei can be seen only after the addition of acetic acid (usually polynuclear or with nuclei irregularly crumbled); sometimes in an alkaline urine they are much swollen and glossy, and in this case also the nuclei are not easily seen. In faintly alkaline, neutral, or faintly acid urine, on the contrary, the pus-corpuscles are often well preserved and sometimes even show active ameboid movements, especially when the slide is slightly warmed. The most important point of differentiation between pus-corpuscles and

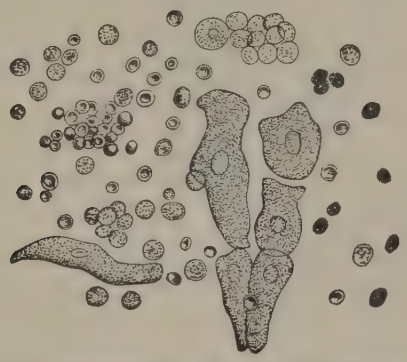


Fig. 266.—Sediment in acid inflammation of the bladder: pus, red blood-corpuscles, and epithelium (after Peyer).

epithelium, especially renal epithelium, is the shape of a number of the nuclei. In the pus-cells the nuclei are usually multiple or very irregularly shaped, never bubble-shaped. This can be best recognized in a stained specimen (p. 682). The size must also be considered. The pus-corpuscles are usually of a diameter of 7 to 10 μ, corresponding to the polynuclear leukocytes from which they arise, whereas the epithelium cells are usually much larger. Figs. 265 and 266 represent the purulent sediment of alkaline and acid inflammation of the bladder or of pyelitis.

Of course, pus-containing urine always contains protein in solution. It is a part of the quantitative estimation (see below) to decide whether the albuminuria, when pus is present, can be explained by the admixture of pus plasma only, or whether we must assume the simultaneous occurrence of a true renal albuminuria. In the latter case the amount of protein is much greater. According to Posner, 100,000 pus-corpuscles in a cubic centimeter correspond to about 1 per cent. of protein. Morphologic elements characteristic of true albuminuria (casts, renal epithelium) will, if present, decide this question. Filtration does not remove

the protein of pus plasma, although this erroneous view has so often been maintained.

Posner formerly suggested that the amount of pus present in the urine could be estimated by counting the number of pus-corpuscles in the centrifugalized twenty-four-hour amount of urine (analogous to counting the red blood-corpuscles) by means of the Thoma-Zeiss counting apparatus. This process is too complicated for practical purposes, so Posner, in a later communication,[1] announced another method of estimating the amount of pus mixed with the urine, or of the amount of sediment in general. The procedure is as follows: The transparency of the urine (the specimen must, of course, be taken from the mixed twenty-four-hour urine) is determined by placing a beaker with flat bottom upon a piece of paper with ordinary-sized print, and estimating the height in centimeters to which it is necessary to fill the beaker, so that in good daylight the print can no longer be read. The degree of transparency is indicated by the thickness of the layer in centimeters. Posner found that a transparency of ½ to 1 cm. corresponded to 40,000 pus-corpuscles per centimeter, and a transparency of 6 cm. to about 1000 pus-corpuscles. Eight centimeters' thickness and above he assumed to indicate normal conditions. Such a quantitative estimation of the amount of pus present is important for estimating the effect of therapeutic interference in cystitis and pyelitis.

BLOOD

Red corpuscles are found in the urine in hemorrhagic inflammation and tumors of the urinary tract and of the kidneys, in traumatic hemorrhage, in calculi, in hemorrhage from congestion, and in hemorrhagic diathesis. The blood-corpuscles appear in the urine partly intact, and partly changed in various ways by the action of the urine. They are most frequently both swollen and minus their pigment, exhibiting only the pale, shadow-like stromata, sometimes as pale disks and sometimes as peculiar, almost invisible, circles. Often the blood-corpuscles break up into small masses of substance containing hemoglobin.

In determining the diagnostic significance of blood-cells in the urine, we meet with the same difficulty as in determining the significance of pus-corpuscles—the difficulty of being sure of their source. In this connection also we must determine whether the amount of protein present in the urine may be explained by the admixture of blood alone, or whether it depends upon renal albuminuria as well. In the latter case the hemorrhage probably comes from the kidneys. If casts with blood-corpuscles adherent or blood-casts also occur in the sediment, the source is certainly a renal hemorrhage. Hemorrhage which leads to the elimination of larger blood-coagula in the urine usually arises not in the kidney parenchyma, but in some part of the urinary tract lower down—either the pelvis of the kidney or the bladder. It should be remembered, however, that in cases of hemorrhage from the renal parenchyma due to nephritis, blood-clots of considerable size may sometimes be found in the urine. A characteristic shape of the coagulum may point to its source from the pelvis of the kidney or the ureter. A considerable amount of blood at the end of micturition probably indicates bladder hemorrhage.

[1] Deut. med. Woch., 1897, No. 40.

Gumprecht[1] claims that if most of the blood-corpuscles are fragments, *i. e.*, disintegrated to small masses, the kidney is generally the seat of the blood-extravasation. In hemorrhage of the bladder, on the contrary, but a few fragmented blood-corpuscles will be found. As concentrated solutions of urea (as low as 8 per cent.) cause fragmentation of the red blood-corpuscles, Gumprecht maintained that the above-mentioned difference is due to the influence of the urea contained in the renal epithelium upon the extravasated blood. The amount of urea in the urine itself is said to be insufficient to produce the change. An objection to this supposition is that it is probable that the blood-corpuscles never come in contact with solutions of urea of the above-mentioned concentration in the kidney. In the opinion of the author, it is more likely that the fragmentation is caused mechanically by the contusion of the blood-corpuscles in the urinary tubules.

CASTS

Urinary casts are characteristic microscopic formations of cylindric form (Fig. 267), which originate in the kidney tubules. They are elimi-

Fig. 267.—Casts in nephritis: *a*, Epithelial; *b* and *b'*, granular; *c*, waxy; *d*, *d*, hyaline; *e*, blood-cast; *f*, cast of white blood-corpuscles; *g*, hyaline cast with epithelium and white blood-corpuscles adherent; *h*, waxy cast with epithelium and red blood-corpuscles adherent (*h* and *b'*, after Bizzozero).

nated in the urine in nearly all cases of renal albuminuria, and infrequently even without albuminuria. Albuminuria may occur without

[1] Deut. Arch. f. klin. Med., 1894, vol. liii.

casts; but, generally speaking, elimination of casts and albuminuria go together. Casts occur most commonly in the various kinds of nephritis, but they may be present in the albuminuria of passive congestion as well as in other types of renal albuminuria. Nevertheless, casts may be absent in all these cases. If the renal albuminuria does not depend upon nephritis proper, this is much more apt to be the case. In nephritis the degree of albuminuria and the number of casts eliminated are usually quantitatively proportional one to the other. Exceptionally, however, and then only for a short time, casts may be absent even with a considerable amount of renal albuminuria. The occurrence of casts without albuminuria (a rare condition) has been observed in very chronic cases of nephritis, in contracted kidney, and in jaundice.

The principal varieties of casts are the following (Fig. 267):

(1) Epithelial casts (*a*), composed of epithelium.

(2) Granular casts (*b* and *c*), granules partly soluble in acetic acid and partly consisting of fat.

(3) Waxy casts (*c*), strongly refractive, sharply outlined, often of a slightly yellow color.

(4) Hyalin casts (*d*), pale, indistinctly outlined, seen readily only with a slanting light.

(5) Blood-casts (*e*), composed of red blood-corpuscles or casts with red cells adherent, yellowish red to brownish, sometimes decolorized.

(6) Casts of white blood-corpuscles (*f*).

Besides these there are many intervening varieties—*e. g.*, hyalin or waxy casts with red or white blood-corpuscles or epithelium adherent (*g* and *h*).

Fatty casts are casts which contain fat in such large quantities that the ground-substance of the cast is entirely obscured. Casts may be composed of pus or of bacteria. Such occur in infections, pyelonephritis, and in the kidney of pyemia. Other casts may become filled with bacteria in infectious conditions of the urinary apparatus, in the kidney itself or in the urinary tract, and even outside the body in urine containing bacteria. In uric-acid infarct of the new-born so-called uric acid casts are found, consisting of spheres of sodium urate. Casts of any variety may become incrusted with urates in a concentrated urine after standing; they then present a peculiar dark granular appearance. They are differentiated from true granular casts by their uneven margins. The urate granulation disappears as soon as the urine is warmed or rendered alkaline.

The length and thickness of casts vary greatly. It is impossible to draw any conclusions as to the source of the casts in the kidney tubules from their diameter, because the diameters of the renal tubules are changed in pathologic affections of the kidney parenchyma. Sometimes the casts present peculiar screw-like twists, but such a peculiarity does not mean that they originate in the convoluted tubules. We require a microscope to see casts properly unless they are very thick and long.

The epithelial casts evidently consist of desquamated epithelial cells which are eliminated adhering to each other. These casts sometimes possess a lumen, and are then spoken of as epithelial "tubules." In a similar way extravasated red corpuscles form the so-called blood-casts, and the leukocytes the white-corpuscle casts. Any of these conglomerations of cellular elements may be so tightly compressed or disintegrated that the cell borders become more and more obliterated. Such changes, the nature of which we do not well understand, may take place in the kidney tubules themselves or in the urine after voiding.

All grades of intermediate forms which still have the stamp of their origin merge without any sharp division into granular and waxy casts in which no nuclei or cell-walls are to be distinguished. The existence of such transitional forms makes it probable that the granular and waxy casts originate as cell conglomerations. In these the epithelium and leukocytes appear to play the chief part, the red corpuscles a much smaller one. This view as to the genesis of the waxy and granular casts is supported by many investigations upon the diseased kidney itself. Formerly the casts which contained no cells, the granular and waxy as well as the hyalin, were considered to be coagulated. Whether this genesis can still be considered, in view of what has already been mentioned, has not yet been certainly decided, but it is not improbable that the hyaline casts are really formed by exudation. It is as yet still unknown by what process the hemoglobin which separates from the blood in solution in hemoglobinuria assumes in the kidney tubules the form of solid casts—the so-called hemoglobin casts. It can, however, be easily conceived that these do not consist solely of hemoglobin, but only represent hyalin and waxy casts infiltrated with hemoglobin.

We have but little accurate knowledge of the chemical nature of casts. Once in a while some cast (especially a waxy one) will give an amyloid reaction, *i. e.*, stain red with gentian violet and brown with iodin, although such a reaction does not indicate any amyloid degeneration of the kidney itself, for, as a matter of fact, in amyloid disease such a reaction of the casts is hardly ever observed.

The importance of finding casts in the urine is due to the fact that they always indicate some pathologic condition in the kidney, and, if accompanied by albuminuria, make it practically certain that the kidney itself is involved. But the change in the kidney need by no means be of a severe anatomic nature. Even slight disorders which produce but a temporary albuminuria may be accompanied by casts, although in small numbers.

For the distinction between nephritic albuminuria, on the one hand, and febrile or congestive albuminuria, on the other, we may lay down the rule that, if casts do occur in the latter, this is the exception. They are almost always merely hyalin. But both the febrile and congestive albuminuria may change to a nephritis without any very sharp borderline.

Little can be claimed for the diagnostic importance of the different varieties of casts. Granular and waxy casts (as opposed to hyalin and epithelial) were formerly supposed to indicate a chronic process; but the idea was wrong. Any and all varieties of casts may be found in every type of nephritis, and even an amyloid kidney does not produce any distinctive type casts (see above). Generally speaking, granular and waxy casts probably owe their peculiar characteristics to the fact that they have remained in the kidney tubules for some time. But that does not necessarily mean a case of chronic nephritis. As a matter of fact, it would probably mean acute nephritis or the acute exacerbations of chronic nephritis, as in such cases the casts remain especially long in the kidneys because the excretion of urine is most interfered with.

MUCOUS CASTS (Cylindroids)

These are peculiar formations which an inexperienced observer may mistake for true casts. They are, however, less distinctly outlined, shaped more irregu-

larly, sometimes flat and tape-like, of smaller diameter, and frequently branching. They probably consist of mucus, *i. e.*, of the undissolved portion of nucleo-

Fig. 268.—Cylindroids (after Peyer).

protein contained in the urine. They are, generally speaking, pale and hyaline, but may be covered with urates, and then appear granular. (Compare p. 688.) They are of no especial diagnostic importance.

TESTICLE CASTS

In spermatorrhea certain formations are sometimes found in the urine which by themselves can hardly be distinguished from hyalin casts. The chemically normal condition of the urine, and the fact that this type of cast appears only in that portion of the urine leaving the urethra first, and is usually accompanied by spermatozoa, will generally suffice to differentiate them from true renal casts.

GONORRHEAL THREADS (Shreds)

In the late stages of acute gonorrhea, when the secretion becomes more of a mucous consistence, and in chronic gonorrhea, even when it gives rise to no other distinct symptoms, peculiar thread-like formations are found floating in the urine. They are up to 1 cm. in length, visible to the naked eye, generally pointed at the end, and of a yellowish to whitish color. Under the microscope we can see that they have a mucoid ground-substance, probably consisting of nucleo-albumin, in which pus-corpuscles and epithelium are embedded.[1] They are probably caused by accumulation of secretion in the longitudinal folds of the urethra, whence they are torn away by the stream of urine.

SPERMATOZOA

Spermatozoa occur in the urine after coitus, nocturnal emissions, and onanism, in spermatorrhea, and after epileptic and other convulsive attacks.

FRAGMENTS OF NEW-GROWTHS AND ELASTIC FIBERS

We may find in the sediment bits of tissue which have been separated from papillomata and carcinomata of the urinary tract or, more especially, of the bladder. Similar bits may be caught in the catheter when irrigating the bladder. If such fragments are large enough to be sectioned and stained, the microscope will quickly determine their nature.

[1] Plate to be found in Peyer, Atlas der Mikroskopie am Krankenbette, 1887, Plates 62 and 63.

The demonstration of elastic fibers is sometimes quite important in the diagnosis of ulcerative processes of the urinary tract (Fig. 277). (See Examination of the Sputum.) The urine is first acidulated to prevent the formation of a phosphate precipitate, and then centrifugalized or allowed to settle. The liquid is then poured off from the sediment, and the latter gently heated with an equal quantity of diluted (10 per cent.) potassium hydroxid. This will destroy most of the morphologic constituents except the elastic fibers. The mixture is then diluted with water and centrifugalized again. If the urine contains a great number of elastic fibers, they may be recognized microscopically without further preparation. Elastic fibers must not be confused with vegetable fibers, which may gain access to the urine from the walls of a dirty vessel. The differentiation is discussed at p. 705—Examination of the Sputum.

MICRO-ORGANISMS

Urine which has been allowed to stand soon furnishes a very favorable medium for the growth of all kinds of bacteria, particularly if the surrounding temperature be raised. The development of these organisms will decompose the urine in various ways. The chemical changes which take place in the urine may lead to the decomposition of any organized admixture and also to deception as to its composition. It is, therefore, important to preserve the urine in a cool place, and to undertake the qualitative examination as quickly as possible after voiding. For this purpose a twenty-four-hour specimen is not necessary. The decomposition of the urine may be checked by adding chemically indifferent antiseptic substances, *e. g.*, several cubic centimeters of coarsely powdered camphor or one-fifth its volume of chloroform water, or the same amount of 0.1 per cent. solution of thymol. For the same reason urine glasses must be kept as aseptic as possible. This is best accomplished by washing them with water and then with a 0.1 per cent. sublimate solution or a 2 per cent. warm soda solution every time after they have been emptied, and then keeping them covered, so that they are not contaminated by the bacteria in the dust of the air.

As we have seen, bacteria are very frequently found in the urine. The microscope will quickly settle the question of their presence in the sediment. A diffuse contamination by bacteria alone may be responsible for a very pronounced turbidity. Such a cloudiness may be distinguished from one caused by unorganized material, as it is affected neither by heat nor by the addition of acids or alkalis. It differs from sediment composed of pus, epithelial cells, or casts in that the latter sediment (1) quickly settles and so clears the upper layers of urine, and (2) is practically always associated with the presence of protein. Shaking a urine extensively contaminated with bacteria often produces a peculiar opalescent, wave-like movement of the cloudiness. Also the opalescent film which appears upon the surface of a urine which has been kept for some time usually consists of bacteria.

The demonstration of bacteria in the urine is diagnostically important only when they occur in freshly voided urine or in a specimen obtained by catheterization. Then they consist either of great numbers of saprophytic bacteria, which are readily seen under the microscope without staining, and which produce abnormal decomposition of the urine within the urinary tract when the latter is diseased (bacteria of

ammoniacal fermentation and bacteriuria), or else of true pathogenic bacteria, which can be recognized microscopically or cultivated upon appropriate media. The latter are found partly in local diseases of the urinary tract, as in certain cases of cystitis and especially in types of acute nephritis, and partly in general infections. They include such organisms as colon bacilli and staphylococci (Fig. 285), streptococci (Fig. 284), gonococci (Fig. 270), pneumococci (Fig. 281), typhoid bacilli, and tubercle bacilli (Fig. 280). In general infections in which bacteria (staphylococci, streptococci, pneumococci) are eliminated in the urine, it is still debatable whether the kidneys and urinary passages are unaffected or whether such elimination is always combined with a lesion of these organs. The microscopic demonstration of these bacteria is really far more important than the culture method of demonstration, because the former excludes the source of error of any incidental contamination, and because it gives more accurate information than the latter as to the quantitative importance of individual species in mixed infections. With a culture it may happen that bacteria of little or no pathologic importance develop inordinately.

The microscopic examination is performed just as with dry-sputum examinations, *i. e.*, dry preparations are prepared by spreading the sediment on cover-glasses (pp. 710 and 715 et seq.). If a specimen of urine is swarming with bacteria, a drop of the urine can be dried and examined like an ordinary dry preparation. If, on the contrary, the specimen of urine contain but few bacteria, it is better to examine a freshly and cleanly prepared sediment obtained by means of the centrifuge. Bacterial suspensions are so difficult to centrifugalize that if other morphologic elements are wanting, the examination will be simplified by first diluting the urine with alcohol. If the urine contain protein or albumoses, the precipitate which results from the addition of the alcohol aids in isolating the bacteria by helping to carry them down in centrifugalizing. Of course, such a precipitate should be merely flaky, otherwise it would interfere with making a good dry preparation. Should the alcohol precipitate large flakes, the urine must first be diluted. Dry preparations are prepared by spreading the sediment thinly upon a cover-glass (just as in sputum) and fixing over a flame. Fixation is, of course, sometimes difficult, because urea is hygroscopic. Hence it is often necessary first to wash the sediment several times with distilled water, centrifugalizing after each washing, or, if necessary, heating for a longer time over the flame, so as to convert the urea into ammonium carbonate. Staining can be accomplished exactly as with sputum preparations (pp. 710 et seq. and 715 et seq.). The bacteria may also be stained by the previously described method of Liebmann. (See p. 682.)

For cultures we must naturally employ perfectly fresh urine, withdrawn by means of a sterilized catheter into sterilized vessels after careful disinfection of the urinary opening. The first urine drawn in this manner must be thrown away, since it may contain bacteria which have been scraped from the walls of the urethra by the eye of the catheter. Even after observing this precaution the urine may become contaminated so that positive conclusions should not be drawn unless there are a large number of colonies.

The demonstration of *tubercle bacilli* in the urine is important for the diagnosis of tuberculosis of the urinary tract (Fig. 280). Dry prepa-

rations of the sediment are employed in the same way as with the examination of sputum (p. 710). In difficult cases the search for the tubercle bacilli may be facilitated by treating the sediment with sodium hydroxid (see p. 714), or tuberculosis may be proved to be present by inoculation experiments upon guinea-pigs. (See p. 714.) A difficulty in such a method is that other pathologic bacteria which occur in the urine

Fig. 269.—Smegma bacilli (× about 800) (after Fränkel).

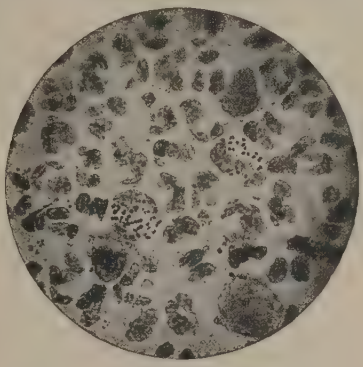


Fig. 270.—Gonococcus (× about 800) (after Fränkel).

may multiply and kill the animal before the tuberculosis can develop. By washing the sediment before inoculation, the danger of such infection is lessened by the removal of toxic urinary substances. The reader should refer to p. 714 and to bacteriologic text-books for the details of performing an inoculation and for the conditions found in the inoculated animals.

Fig. 271.—Echinococcus elements: 1, Free scolices: *a*, rostellum projected; *b*, rostellum withdrawn; 2, hooklets; 3, membrane (× cross-section) (after Heller).

The so-called *smegma bacillus* (Fig. 269 et seq.) has been so frequently confused with tubercle bacilli as often to lead to an erroneous diagnosis of urogenital tuberculosis. The smegma bacillus, as described by Alvarez and Tavel, occurs very frequently in the preputial fold of the male and in the folds above the female clitoris. In the specific staining for tubercle bacilli they also are stained (p. 712). From their location they can easily contaminate the urine and multiply in it outside of the body (?). These parts should, therefore, be washed very carefully before the urine is passed or before catheterization.[1]

[1] Runge and Trautenroth have shown that the urine obtained by catheterization after carefully cleansing the external orificium urethræ is always free from smegma bacilli.

The smegma bacilli differ from the tubercle bacilli in being more slender and not granular, and not exhibiting the characteristic groupings of the tubercle bacilli. (See Figs. 269 and 280.) Finally, when the stained preparations are afterward treated with HCl alcohol for from five to ten minutes, the smegma bacilli become decolorized, but not the tubercle bacilli. Grette recommended combining the counterstaining effect of methylene-blue with the decolorized action of the alcohol.[1] He stains as ordinarily with carbol-fuchsin, and after washing with water he treats the specimen with a concentrated alcoholic solution of methylene-blue (without acid). With this method the tubercle bacilli remain red, whereas all the rest of the preparation, including the smegma bacilli, is stained blue. Another difference between them is that Gram's stain decolorizes the smegma but not the tubercle bacillus. Finally, the tubercle but not the smegma bacilli are changed to formations like strings of pearls, resembling streptococci, by excessively heating the dry preparation, *i. e.*, by passing it perhaps ten times through the flame. Compare also the staining method recommended by Pappenheim for distinguishing tubercle bacilli from smegma bacilli in the sputum. The employment of Ebner's decolorizing fluid will also prevent the confusion of these bacilli. (See p. 712.)

The presence of gonococci in the urine sediment is also of diagnostic interest. (See Fig. 270.)

Fig. 272.—Embryos of Filaria sanguinis: Length, 0.0075 to 0.21 mm.; thickness, 0.004 to 0.36 mm. (after Scheube).

Fig. 273.—Eggs of Distomum hæmatobium (Bilharzia hæmatobia): Length, 0.12 mm.; breadth, 0.05 mm. (after Bilharz).

The *bladder catarrh* and *pyelitis* which may complicate gonorrhea never depend upon a pure gonorrheal infection, but upon secondary infections of the urinary tract with other organisms. At the same time, in such cases, if the disease has not been entirely cured, pus-corpuscles which contain gonococci are sometimes found in the sediment. They have probably become mixed with the urine from the urethra. Fig. 270 shows the characteristic arrangement of the gonococci in the interior of the pus-cells. A diagnosis of gonorrhea is permissible only when this characteristic intercellular arrangement has been recognized, because the same biscuit-like grouping so characteristic of diplococci is also seen with the ordinary staphylococci. Another characteristic of gonococci is that they do not grow upon ordinary culture-media.

Braatz[2] found actinomycosis granules in a case of actinomycosis of the urinary tract (Figs. 292 and 293).

In diabetic urine a rapid yeast growth is sometimes produced by the presence of yeast fungi. The sugar becomes fermented, carbon dioxid bubbles are formed, and yeast spores settle in the sediment. Hence, the demonstration of yeast fungi in the urine may suggest the diagnosis of diabetes; but even non-saccharine urine may exhibit yeast-like fungi.

[1] Fortschr. d. Med., 1896, No. 9.
[2] Petersburg. med. Woch., 1888, No. 13.

ANIMAL PARASITES

Echinococcus of the urinary tract and of the kidneys may cause fragments of echinococcus cysts and hooklets or whole daughter cysts to be voided in the urine (Fig. 271).

Embryos of Filaria sanguinis (Fig. 272) are found in the urine in the tropic hematochyluria, and the eggs of Distomum hæmatobium (Bilharzia hæmatobia, Fig. 273) in the Egyptian hematuria.[1] It remains to be mentioned, finally, that in rare cases the trichomonas is found in the urine in disease of the urinary tract. This species is probably identical with that occurring in the intestine (Trichomonas intestinalis; compare p. 518 and Fig. 216).

EXAMINATION OF THE SPUTUM

Expectoration, or sputum, is what is discharged by coughing or clearing the throat. It is composed of the secretion or exudate from the respiratory mucous membrane of the nose, pharynx, and trachea down to the finest bronchi and alveoli; of material which has reached the respiratory tract from neighboring regions (pus of abscesses and empyema); of blood derived from somewhere along the respiratory tract; and, finally, of material from the buccal cavity or from any part of the digestive tract. Macroscopic and microscopic foreign bodies which have entered the respiratory system from without are usually discharged in the expectoration.

On account of its numerous sources of origin, the composition of the sputum is very complex and of great symptomatologic importance. The sputum is not always expectorated. Small children swallow their sputum; and occasionally adults do the same, as the result of bad habits, lack of practice in expectorating, or of impaired consciousness. Its help in diagnosis is then lost. Some of these adults and most older children can be taught to expectorate, or a reflex expectoration may be incited by touching the base of the tongue, epiglottis, or uvula with a tongue depressor. Sputum may be obtained from children by introducing a finger wrapped with gauze well into the throat. The resulting cough reflex will bring up sputum, which will stick to the gauze. For diagnostic purposes, the expectoration for twenty-four hours is collected most conveniently in a transparent sputum cup.

AMOUNT OF SPUTUM

The amount of sputum may vary greatly, depending upon what process produces it. Some pulmonary patients, in spite of violent coughing, expectorate only a small quantity, and that usually very tenacious (dry bronchitis, incipient phthisis). Others may expectorate large quantities during the day, or even at one time (in certain types of chronic bronchitis sometimes called bronchorrhea, in advanced pulmonary tuberculosis, in bronchiectasis, in pulmonary edema, in pulmonary hemorrhages, and in perforation of abscesses or an empyema into the air-passages). The special characters of these various types of sputum will be discussed later on.

[1] Rüttimeyer, Mittheilungen aus kliniken und medicinishen Instituten der Schweiz, 1894, vol. i.

CONSISTENCE OF THE SPUTUM

The consistence of the sputum bears a certain relation to its amount. If very abundant, a sputum is usually less tenacious than if scanty. Ordinary sputum is mucoid; it may, however, be either serous, purulent, or bloody. The peculiar mucoid (slimy) consistence of sputum depends largely upon the amount of mucus it contains, since the mucin-like substances excreted from the respiratory mucous membrane form a considerable portion of the expectoration.[1] The stickiness of the sputum also is partly due to mucus and partly, in some cases, to its protein content, especially the sputum of croupous pneumonia, the viscidity and tenacity of which are largely due to the amount of nuclein contained.

REACTION OF THE SPUTUM

The reaction of fresh sputum is generally alkaline. It may become acid, after standing for some time, from bacterial decomposition.

COLOR AND TRANSPARENCY OF THE SPUTUM

The color of the sputum varies decidedly. Pure *mucoid* or *glassy sputum* may be perfectly colorless, but its consistence prevents its being easily mistaken for saliva. Admixture of white blood-corpuscles makes this slimy secretion more and more yellow or greenish, and also cloudy and opaque. It is not clear why the color in one case is more yellow, and in another more greenish, any more than in the case of pus. But as the more intense inflammations are usually associated with the transudation of red blood-corpuscles, it seems fair to assume that the green derivatives of blood-pigment usually produce the greenish pus color. (See later with reference to other causes of green discoloration of the sputum.)

A *mucopurulent sputum* consists of an admixture of masses of pure mucus with masses of pus, or of a moderate but uniform admixture of the two elements, the whole appearing but slightly clouded. *Purulent sputum* is the next step in such admixtures. Its consistence is still mucoid, unless composed of pure pus (either thick or thin) derived from an abscess or from the perforation of an empyema, and expectorated as such without any mucus.

Serous sputum is another type of colorless expectoration. It differs from the pure mucoid or glassy sputum in its very liquid consistence and foamy appearance. It occurs in pulmonary edema, and in the very rare perforation of serous pleural exudates into the lung. Serous sputum is frequently slightly tinged with blood.

Sputum has a slightly reddish color whenever mixed with blood. In some cases the sputum consists of pure blood; in other cases it contains only a slight admixture, producing a salmon color. Between these two extremes all sorts of transitional forms occur. Hemorrhagic sputum is observed in traumatic and tuberculous hemorrhages from the lungs, in hemorrhagic infarctions of the lungs, in pneumonia (especially in croupous pneumonia), in gangrene of the lung, in tumors of the

[1] The mucus of the respiratory apparatus appears to be composed mostly of true mucin (Cohnheim, Chemie der Eiweisskörper, Braunschweig, Vieweg, 1900; F. Müller, Beiträge zur Kenntnis des Mucins, etc., Zeit. f. Biol., vol. xlii).

lung, and finally in congestion of the pulmonary circulation. The different shades of blood containing sputa will be described below.

Certain derivatives of blood-pigment produce in the sputum very similar shades to that of bloody sputum proper. Rusty sputum, the most common type in pneumonia, is an instance. The coloring-matter is here partly unchanged blood, partly, however, certain derivatives of the blood-pigment, about which little is as yet known. Among these may be mentioned methemoglobin or bilirubin (hematoidin). Peculiar lemon-colored and dirty green to grass-green shades, the effect of further chemical transformation of the blood-pigment, are infrequently observed in pneumonia sputum. All these variations are analogous to the changes of blood-pigment observed in subcutaneous ecchymoses. Such sputa respond to Gmelin's test for bile-pigment (see p. 575 et seq.), and also contain bilirubin. Lemon-yellow and greenish sputa in pneumonia are frequently called icteric sputum. This name is, however, justifiable only when there is general jaundice or, at least, some icteric discoloration of the conjunctivæ, or when bile-pigment is contained in the urine. A peculiar light-brown shade characterizes sputum which contains abundant cells of heart disease. (See Plate 8, Fig. 3.) Here amorphous blood-pigment is found encapsulated in the pulmonary epithelium. The brownish or ochre-like color of the sputum which is occasionally observed in destructive processes of the lung, especially in pulmonary abscesses, or in a liver abscess which has perforated into the lung, is due to hematoidin crystals, apparently identical with bilirubin. (See Fig. 278, *d*, p. 707.) In the expectoration from a liver abscess the hematoidin or bilirubin crystals are derived not from the blood, but from the admixture of bile with the pus. The bitter taste noticed by patients when expectorating such sputum depends upon the presence of biliary salts. Gmelin's reaction for bile-pigment will not differentiate the source of the hematoidin or bilirubin, as they react in the same way, whether derived from blood or from bile.

True icteric sputa, such as has been observed in certain cases of pneumonia, which are complicated by jaundice, or with any other pulmonary affections with jaundice (see p. 42 et seq.), may present various shades of color, due to the oxidizing of bilirubin. Yellow and then dirty-green shades are the most common.

A rather different type of green sputum has been described in lung tumors, but the nature of the pigment in question is as yet unknown. The sputum in certain pulmonary tumors (chloroma; see Examination of the Blood, Leukemia) which belong to the lymphadenomata is greenish in color. Hence a greenish sputum in a supposed tumor of the lung would suggest a chloroma; but green sputum has been observed in cases of carcinoma. It is, however, usually easy to diagnose chloroma from other symptoms, especially the involvement of the bones of the skull and the frequently associated blood-picture of leukemia. The pigment of chloroma dissolves in alcohol. Too much attention has probably been devoted to the green sputum in tumors of the lung, because, as we shall see, the multiplication of chromogenic bacteria may cause a greenish coloration of sputum outside of the body in almost any affection.

Other striking colorations of sputum have been observed from the admixture of inhaled dust-particles. Black sputum belongs to this class. Its pigment is due to inhaled coal-dust or soot, of which, as is well known, normal lung pigment consists. A small portion of the

carbon is free in the sputum; the larger part is contained in the interior of round or oval epithelium and white blood-cells. (See p. 704.) Particles of soot look like amorphous granules, but under the microscope we can frequently recognize the vegetable structure of the larger particles of carbon. These are usually not contained in the cells, but are found free. The gray or blackish discoloration of such sputa, as well as the degree of lung pigmentation, depends chiefly upon the individual's occupation. The sputa of coal-miners and workers in coal are frequently intensely black (anthracosis of the lung). Other *pneumonokonioses* (*i. e.*, changes in the lung produced by the inhalation of dust) are associated with peculiar coloration of the sputum. Workmen (*e. g.*, in polishing mirrors) who breathe the dust of oxid of iron (English-red, caput mortuum), and who have thereby acquired siderosis of the lung, may expectorate an ochre-colored sputum. The reddish particles are, for the most part, inclosed within the cells. To demonstrate siderosis from the sputum, add hydrochloric acid and a solution of ferrocyanid of potash; Berlin blue will then be formed. Blue sputum has been observed in men working in ultramarine.

These colorations of the sputum are not due to the pigment which has impregnated the lung, for whatever pigment particles are deposited in the lung probably never leave it; they should rather be considered as coeffects of the same cause, viz., inhalation of dust. Only the dust which has been recently inhaled, and which has not penetrated the interior of the pulmonary tissue, is expectorated. Consequently the characteristic coloration of the sputum will disappear soon after the patient gives up the occupation that produced it, although the pneumonokoniosis will persist. Colored sputum should be considered rather as a sign of the inhalation of dust than of pneumonokoniosis. Where the characteristic discoloration of the sputum continues or reappears after the individual has been removed for some length of time from the specific dusty atmosphere, it generally means that some destructive process, usually tuberculosis, is added to the pneumonokoniosis.

The "gluing" or "smearing" of the respiratory passages, described by Gerhardt and Lublinski,[1] which occurs in bakers and millers should be mentioned. Here paste-like masses are expectorated. It is due to the inhalation of flour.

The manifold colorations of the sputum due to admixtures from without, and not from the air-passages, should be mentioned, *e. g.*, when patients take milk, eggs, claret, coffee, chocolate, licorice, or some colored medicine before expectorating, the sputum is apt to become discolored in the mouth. A green discoloration of the sputum is sometimes due to the growth of certain chromogenic bacteria, especially the Bacillus virescens.[2] Yellow, bluish, and reddish sputa of probable bacteriologic origin have also been observed. The parasite of "blue pus" (Bacillus pyocyaneus) probably thrives in sputum under certain conditions.[3]

AIR CONTENT OF THE SPUTUM

Sputum is often more or less distinctly foamy or frothy, due to the presence of air. Other things being equal, the amount of air contained in sputum is greater the finer the bronchi from which it is derived. This is because air is most easily incorporated with tiny masses of spu-

[1] Gerhardt, Centralbl. f. inn. Med., 1896, No. 20; Lublinski, ibid., 1896, No. 28.

[2] See Frick, Virchow's Arch., 1889, vol. cxvi, p. 226.

[3] [Norris isolated from the sputum of a case of chronic bronchitis a bacillus which could not be differentiated from the Bacillus pyocyaneus. This sputum when first expectorated was colorless, but developed an intense greenish color upon standing less than three hours. The literature contains a number of similar instances.—Ed.]

tum, as they are being collected into large masses, while passing from the smaller to the larger bronchi. The consistence of the sputum is also of importance. Thin sputum is usually very frothy. Thick, tough sputum is less so. The amount of air contained in the sputum can be readily recognized by its specific gravity. Air-containing sputum will float on the water in a sputum-cup; airless sputum will sink. The sinking of sputum (sputa fundum petentia) has been considered a proof of its derivation from a cavity of the lungs. Evidently, sputum derived from the pus of pulmonary cavities will ordinarily contain but a slight amount of air; but so may purely catarrhal secretion from the larger bronchi, so that this test is of slight diagnostic value, and then only in connection with other signs.

SPUTUM STRATA

Sputa which settle in layers in the cup are observed chiefly in bronchorrhea (chronic bronchitis with abundant secretion), in bronchiectasis, in putrid bronchitis, and in gangrene of the lung. The sputum is profuse and very fluid in all these conditions, and, besides, is rich in morphologic elements, pus in the one, shreds of parenchyma in the last named, gangrene. There are usually three layers—an uppermost, aërated and floating portion; a middle, fluid layer, consisting chiefly of purulent serum or mucoid fluid; and a third layer, the sediment, which consists of pus-corpuscles, gangrenous shreds of lung tissue, and molecular lung detritus.

ODOR OF THE SPUTUM

Fresh sputum rarely has any particular odor; but upon standing a short time it may acquire a disagreeable odor, due to the action of bacteria. Freshly expectorated sputum has a very strong offensive odor in purulent bronchitis, in many cases of pulmonary tuberculosis, and bronchiectasis and pulmonary gangrene, and very frequently in pulmonary abscess and in empyema which perforates the lung. The disagreeable odor in these cases arises from the growth of putrefactive bacteria even before the expectoration of the sputum. Stagnation of the secretion in cavities favors the processes of decomposition. The foul odor of the contents of the lung is usually imparted to the exhaled breath, where it may even be more distinct than in the sputum itself. This is frequently noticed in consumptives. The peculiar carrion-like odor of the breath so characteristic of this disease will sometimes point to pulmonary tuberculosis even before definite pathologic signs are plainly evident in the chest, and while the sputum may be remarkably free from odor. We should then naturally suspect that the foul odor came from the mouth, although the futility of cleansing the mouth with such deodorants as permanganate of potash or dioxid of hydrogen proves that the offensive odor originates in the depths of the lung. This is very likely due to the fact that the warm air in the lung takes up odors more readily than the external air at room temperature. Besides, sputum may very rapidly lose its odor upon standing from evaporation of its upper layers. The same is true of the fecal vomitus in intestinal obstruction. It seems to the author probable, and his idea is confirmed by others, that consumptives with this char-

acteristic odor usually have cavities (even if quite small) in which the secretion stagnates.

The sputum may have a peculiar odor after the administration of myrrh, oil of turpentine, ether, alcohol, paraldehyd, etc. It has been assumed that these substances are partly eliminated by the lungs.

CHARACTERISTIC GROSS APPEARANCES OF THE SPUTUM AND ITS ADMIXTURES

Many sputa appear to the eye perfectly homogeneous—pure mucous, pure purulent, pure bloody, etc. But sometimes not only may the sputa from one patient vary, but differences can be distinguished in each individual expectorated mass. Particularly in mucopurulent sputum the particles of mucus and pus may alternate. From the quantity of these individual constituents we can judge more or less correctly whether the sputum arises from a larger or a smaller bronchus.

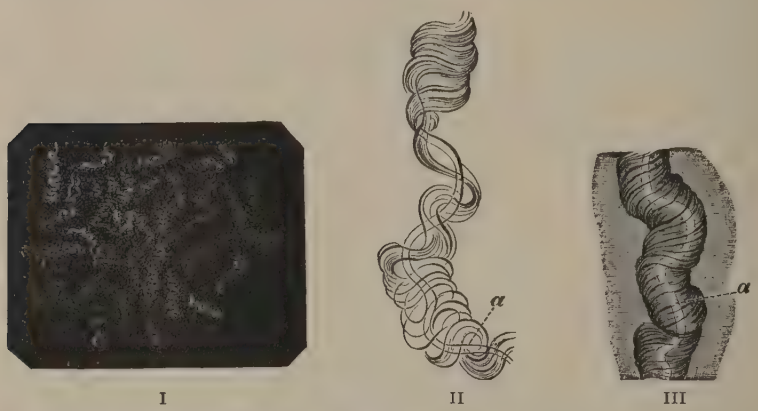


Fig. 274.—Curschmann's spirals: I, Natural size; II and III, enlarged: *a*, *a*, a central fiber (after Curschmann).

A peculiar fine, flocculent, shaggy appearance of purulent sputum is very characteristic of the slow emptying of a pleural empyema or of a pulmonary abscess. The flocculi can be best seen if the sputum be suspended in water. They are probably due to the fact that the pus is pressed into the shape of shreds or strands in being squeezed through the narrow seat of perforation. These shreds become surrounded by mucus, and are then no longer confluent.

To detect other admixtures which exhibit a microscopic difference from the main bulk of the sputum, it is advisable to examine a small portion of the sputum upon a plate one-half of which has been painted with black enamel paint, so that the background may be either black or white, as desired. In this way it is easy to select ropy, fibrous, generally dirty, dark particles or larger grayish-black shreds characteristic of necrotic lung tissue. If elastic fibers (Fig. 277) be detected by the microscope, the diagnosis is confirmed. These, however, may be absent

in gangrene of the lungs (p. 706). Bits of necrotic cartilage in ulcerative processes of the bronchi, trachea, or larynx, and tumor fragments in tumors of the lungs or bronchi, may be detected in the same way.

"Dittrich's plugs," yellowish-white bits the size of a mustard seed, are very conspicuous when looked for over a dark background. They come from the smaller bronchi in putrid diseases of the lungs, especially in putrid bronchiectasis and in pulmonary gangrene. Microscopically, they consist of clumps of bacteria and crystals of fatty acids (compare Fig. 278, *a*). They have a very intense and disagreeable odor.

Similar plugs may he seen mixed in the sputum in follicular tonsillitis from the crypts of the tonsils.

"Dittrich's plugs" should not be confused with the spiral formations described by and named after Curschmann. These are represented in Fig. 274: I, natural size; II and III, slightly magnified. They consist of long or short, worm-like formations, 1 and 2 cm. long and about 1 mm. thick, more or less opaque, and usually suspended in a glassy menstruum. They are shiny, viscid in consistence, are visible to the naked eye, and are composed of shreds twisted into a spiral. They are only rarely branched. Some of them exhibit a central, more strongly refractive fiber in the axis of the spiral (Fig. 274, II, *a* and III, *a*). Other formations which resemble these central fibers occur in sputum, but they are isolated and not surrounded by spirals. A. Schmidt[1] showed, by staining, that Curschmann's spirals and the central fibers consist of a mucin-like substance and not of fibrin, as was formerly supposed. They are not so dense as the shreds of fibrin which occur in the sputum. These spirals of Curschmann are portions of the secretion or exudate which forms in the finest bronchi as the product of a so-called *bronchiolitis exudativa*. Curschmann's spirals are more or less characteristic of asthma sputum. After the end of a typical attack they are sometimes found in extraordinary numbers. We must not, however, suppose that Curschmann's spirals are pathognomonic of asthma, for not only do cases of asthma occur without spirals, but spirals may be found in the sputum of a bronchitis without asthma. They are sometimes found in croupous pneumonia, in which case there is a very good opportunity to distinguish them from bits of fibrin. When strongly magnified, the spirals will frequently be found to contain white blood-corpuscles and Charcot's crystals (Fig. 278, *e*). These leukocytes, particularly in cases of bronchial asthma, are conspicuously, for the most part, mononuclear, and contain eosinophilic granules.

Curschmann's spirals can be preserved in glycerin. Their mode of origin is by no means definitely known. Doubtless their shape is due to the screw-like movement of the mucus while passing through the bronchi. Personally, the author prefers to consider that this spiral motion is caused by the movement of the cilia of the bronchial epithelium, although we do not yet know whether the direction of the motion of the cilia in the bronchial mucous membrane of man is spiral or not. But even if the cilia should be proved to vibrate in the axis of the bronchi, the progress of the sputum from the lateral branches would exert a tangential force and so cause a twisting motion to the ball of sputum. Senator assumes that the screw-like shape of these structures is brought about by physical means, and that it is analogous to the spiral-like mass of a salve which is forced out of a compressible tube by pressure—the reason for which is that the resistance over the entire circumference is never exactly equal and so its contents necessarily move laterally, and secondarily a twisting motion results.

[1] Zeit. f. klin. Med., 1892, vol. xx, p. 476.

Formations consisting of fibrin may be found in the sputum under various conditions. They are easily recognized by their white color, by their tenacious consistence, and sometimes by their shape. In diphtheria of the pharynx, larynx, and trachea, the expectorated fibrinous pseudomembranes consist of shapeless masses or casts of these organs. Diphtheria not infrequently reaches as far as the bronchi, and branching, tree-like bronchial casts may be expectorated. They are readily recognized and are important in diagnosing the extension of the disease to the lungs, and so determining the prognosis. Similar branching bronchial casts are observed still more frequently in croupous pneumonia, because the bronchial mucous membrane usually participates in the fibrinous inflammatory process. Fig. 275 represents a cast of this sort. Large numbers of such casts are often contained in the sputum of pneumonia. They look like white strands or shreds. To investigate their nature more accurately, they should be isolated by shaking the portion of sputum which contains them in a test-tube with water. All other formations lose their shape, whereas these casts float about in the water. These tree-like formations may be solid or hollow. Similar formations are found in the sputum of patients with fibrinous or croupous bronchitis. The etiology of this disease has not been investigated carefully. Its course is usually chronic, very rarely acute. The sputum is more or less blood-tinged, and not infrequently contains beautiful branching casts of very large bronchi. Hochhaus has proved that some of these casts (coagula) in the disease under discussion are composed of mucin. Under the microscope these fibrinous casts show the ordinary coarse structure of fibrin and the same power of refracting light. Like Curschmann's spirals, they often contain Charcot's crystals (Fig. 278, *e*). Fibrin coagula can be distinguished both macroscopically and microscopically from mucous constituents of the sputum by their swelling and becoming more translucent after the addition of acetic acid. If fresh fibrin be submerged in dioxid of hydrogen, gas will develop much more quickly than in the case of mucus (catalytic action of the peroxydases of fibrin).

Fig. 275.—Fibrinous bronchial casts.

Foreign bodies are sometimes aspirated. They may even remain in a bronchus for years without causing any symptoms, and finally be expectorated. There are cases reported where foreign bodies, such as teeth, cherry-stones, etc., have been expectorated after having been ten and even nineteen years in the lungs.

Calcareous concretions are sometimes, but very rarely, formed in the lungs during chronic infections. They may be finally coughed up (lung-stones, pneumoliths).

Occasionally such concretions form about aspirated foreign bodies,

in other cases, the histologic examination shows they are made up of necrotic and calcified lung tissue (calcified tubercles). There are recorded cases where lung-stones in great quantities have been coughed up. On the chemical composition of lung-stones, see Stern.[1]

Very rarely entire daughter cysts of pulmonary or hepatic hydatids reach the bronchi, and so appear in the sputum, in addition to microscopic constituents of the echinococcus (Fig. 271). Hair and teeth are sometimes found in the sputum following the perforation of a dermoid cyst of the mediastinum into the bronchi.

MICROSCOPIC EXAMINATION OF THE SPUTUM

In many cases this purpose can be satisfactorily accomplished by placing a small particle of the sputum upon a slide and then pressing down with a cover-glass. To recognize some of the constituents, the specimen must first be treated with reagents and stains (see later). The sputum should, however, first be examined just as expectorated. This process is frequently neglected. The presence of fungi or of crystals in the sputum, the nature of many cellular elements, etc., can be recognized only in such a fresh preparation, or, at least, much more easily recognized there.

Most sputa consist microscopically of a groundwork of mucoid material of indefinite structure in which pus-corpuscles a reembedded. The number of the latter determine the more or less purulent nature of the sputum. The character of these corpuscles varies considerably. Their size is from 7 to 10 μ. They are more or less granular. The granules consist partly of protein material (neutrophilic, rarely eosinophilic, granules; see Examination of the Blood, Leukocytes), partly of fat, partly of extraneous débris, identical with that of so-called lung epithelium (see below). Bacteria are also found inclosed in leukocytes, especially pneumococci. Like polymorphous leukocytes, from which they originate, these pus-corpuscles usually possess one irregular nucleus or several nuclei. In stained preparations (hematoxylin) the nuclear substance never appears as a vesicle, but is compact. (For the presence of eosinophilic mononuclear cells see p. 708 et seq.)

Epithelial cells are also found in sputum. They differ from pus-corpuscles in exhibiting a single, rather large vesicular nucleus. Various types of epithelium are found in the sputum. Their demonstration and recognition are of especial importance for determining the origin of a catarrhal expectoration. First of all, there is *squamous epithelium*, derived from the mouth, the pharynx, and a portion of the larynx, especially the true vocal cords (Fig. 276, *i*). There is *cylindric epithelium* (Fig. 276, *f*, *h*), derived from the deep-seated bronchi or from the nose, and represented by beaker-shaped and ciliated cells, although, of course, many of the latter have lost their cilia. They are rarely very numerous, except perhaps in a fresh bronchial catarrh. In the latter stages of catarrh they are almost completely supplanted by leukocytes.

Besides epithelium derived from the upper portion of the respiratory tract, there is the so-called *pulmonary* or *alveolar epithelium* (Fig. 276), *a*, *b*, *c*). These are oval cells, 20 to 50 μ in diameter, with one or several

[1] Deut. med. Woch., 1904, No. 39, and Carlyon, Brit. Med. Jour., 1890, ii, p. 1474.

nuclei and various substances inclosed within them. The latter consist of: (*a*) normal lung pigment, *i. e.*, carbon (Fig. 276, *a*); (*b*) fat; (*c*) so-called myelin granules or drops, which are pale, irregular bodies of considerable size, showing concentric layers, and resembling the myelin globules of the central nervous system (see below as to their origin); (*d*) granules or scales of brown or yellow pigment, in all probability derived from blood-pigment (heart-cells; Plate 8, Fig. 3); (*e*) hematoidin crystals. The same cell may inclose a variety of inclusions. We do not know whether these cells, as claimed by Bizzozero, are derived exclusively from the epithelium of the pulmonary alveoli, or whether some of them may not be cells from the epithelium of the upper air-passages, or mononuclear leukocytes, enlarged by their contents.

Fig. 276.—Different morphologic elements of the sputum: *a*, *b*, *c*, Pulmonary or alveolar epithelium—*d*, with normal lung pigment (carbon); *b*, with fat-globules; *c*, with myelin granules or drops; *d*, particles of pus; *e*, red blood-corpuscles; *f*, cylindric beaker-shaped bronchial epithelial cells; *g*, free myelin granules; *h*, ciliated epithelium of different kinds from the nose, altered by coryza; *i*, stratified epithelium from the pharynx (after Bizzozero).

The character of the epithelial cells found in the sputum makes it possible to locate the portion of the respiratory tract from which the microscopic specimen was originally derived.

The myelin drops or granules above mentioned are often found free in the sputum. According to the investigations of A. Schmidt, they should be considered a product of normal secretion of the mucous membrane of the respiratory system. They make up the larger part of the *morning sputum*, which is swallowed by the majority of people. Chemical examinations by A. Schmidt and F. Müller have shown that the myelin of sputum consists largely of protagon, with which is mixed a small amount of cholesterin and lecithin.

If "heart-cells" occur in large numbers in the sputum, we are justified in assuming definite anatomic changes in the lung. These cells are filled with yellowish-brown pigment-granules. (See Plate 8, Fig. 3.) They have been called the "cells of heart disease," because they are found in the sputum in brown induration of the lung from cardiac lesions, especially those of the mitral valve. They are of real diagnostic importance in this condition if found in considerable numbers for a con-

siderable length of time without the existence of an infarction or of pneumonia. In the sputum of the two latter conditions these cells are also found as well as after hemoptysis. Their origin is explained as due to these cells having engulfed the remains of red corpuscles extravasated into the alveoli. Sputum containing many of these cardiac cells may sometimes appear slightly reddish brown.

Whenever the bloody character of a sputum is doubtful, a microscopic examination will usually determine the presence of the red corpuscles. They may have preserved their normal appearance, or they may be altered in various ways. They may disintegrate into distinct and separate accumulations of hemoglobin, and, later on, become amorphous or crystalline hematoidin, or sometimes the coloring-matter may be entirely dissolved.

Wherever lung tissue is considerably destroyed by any pathologic process, elastic fibers are apt to be found in the sputum. They form the resisting portion [the framework.—Ed.] of the pulmonary parenchyma

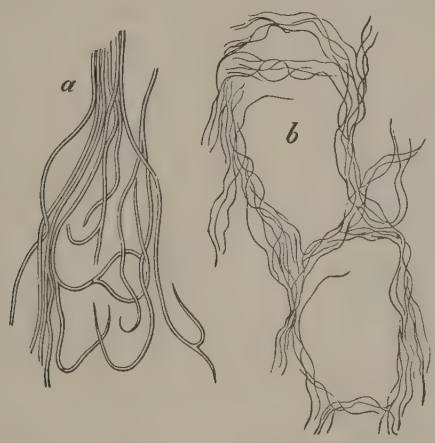


Fig. 277.—Elastic fibers from the sputum (after Bizzozero).

(Fig. 277). Their presence in the sputum proves beyond a doubt the occurrence of some destructive process in the lungs, hence their importance in the early diagnosis of tuberculosis of the lungs before the tubercle bacillus was discovered. Even now the presence of elastic fibers may decide the diagnosis if we are unsuccessful in our search for tubercle bacilli. Elastic fibers are also found in pulmonary abscess and gangrene in greater or less number according to the rate of disintegration.

The fibers can usually be detected if a thin layer of fresh sputum be examined microscopically. If they are so scarce that they cannot be found in this way, the following procedure is recommended: About 10 cc. of sputum are boiled in a small porcelain dish with an equal quantity of 10 per cent. KOH. The mixture should be well stirred during the boiling. When it becomes homogeneous, it is diluted with about four times as much water, well shaken, and then centrifugated or allowed to stand in a pointed glass. If any elastic fibers be present, they may be picked up from the sediment with a pipet and then examined under

the microscope. After subjecting elastic fibers to KOH, they are usually somewhat less sharply outlined and slightly swollen.

When present in considerable quantity, they are easily recognized by their alveolar arrangement (Fig. 277, *b*). Beginners are liable to confuse isolated elastic with vegetable fibers, but most of the latter have a large diameter, and are much less plainly wavy. A beginner might be confused by the resemblance which thread-like collections of bacteria, or even the mycelium of fungi, bear to elastic fibers, but a higher magnification or staining will readily differentiate them.

R. May has described a very convenient method of staining elastic fibers with orcin. The method is useful in doubtful cases. The technic will be found in May's original article.[1]

Weigert has also given an excellent method for staining elastic fibers in sections by means of fuchsin. The author recommends its employment for the demonstration of elastic fibers in the sputum. The cover-glass smear is first dried, and then fixed with absolute alcohol or formalin. A few minutes will suffice for fixation if alcohol be employed. If formalin be used, the specimen should be left for an hour in a 4 per cent. aqueous solution of formaldehyd, and then washed off with absolute alcohol. The staining fluid is prepared as follows: Two hundred cc. of an aqueous solution of fuchsin (1 per cent.) and resorcinol (2 per cent.) are brought to the boiling-point in a porcelain dish; 20 cc. of liquor ferri sesquichlorati are then added, and the mixture constantly stirred and boiled for three to five minutes, when a muddy precipitate will form. The mixture is then cooled and filtered. The filter and the contained precipitate are dried, and again placed in the same porcelain dish, which will also contain some of the precipitate. Two hundred cc. of 94 per cent. alcohol should then be added, and the mixture boiled over a water-bath and constantly stirred. During this procedure great care must be exercised to avoid ignition of the vapor. The fluid is cooled, and enough alcohol is added to bring the amount up to 200 cc., after which 4 cc. of hydrochloric acid are added. The cover-glasses should remain in this fluid from twenty minutes to an hour, after which they are washed with alcohol, cleared in xylol, and finally examined in Canada balsam.

Dr. J. Bamberger, of Kissingen, has recently informed the author that he and L. Michaelis have used the Weigert stain, in the following way, for the determination of elastic tissue in the sputum, and have found it trustworthy: The sputum is pressed, and equally distributed between two slides, by rubbing them backward and forward on one another. Large amounts of sputum, and especially the suspicious looking portions, should be selected. A slide is then dried in the air and completely submerged, without fixation, in a Coplin jar filled with Weigert's fuchsin solution (see above). The 94 per cent. alcohol of the Weigert solution suffices for the fixation.

The preparation is left in the stain for one-half to three-quarters of an hour, is then gently washed with alcohol containing 3 per cent. of HCl, and put in a Coplin jar containing 3 per cent. HCl-alcohol until no more color is given off. It is then removed, dried in the air (heat makes the color fade), and examined in cedar oil with a low magnification. One can take large amounts of sputum, since absolutely nothing but elastic tissue is stained.

Some cases of incipient phthisis which otherwise can hardly be recognized may show the presence of elastic fibers.

It is a peculiar fact that in some cases of gangrene of the lung, but not in all, elastic fibers of the lung are absent in necrotic pieces of lung tissue, recognized microscopically as such. In such cases the elastic fibers have been destroyed by a trypsin-like ferment formed by bacteria which grow in the gangrenous tissue. Even then the author has always found them after a sufficiently thorough search.

Fragments of neoplasms of the lung which are sometimes seen in the sputum (p. 701) are best recognized in microscopic sections.

Crystals Observed in the Sputum (Fig. 278).—Crystals occur in the sputum almost exclusively when the latter has remained in the

[1] Deut. Arch. f. klin. Med., vol. lxviii, parts 5 and 6, p. 427.

body for a considerable length of time. Crystals of fat or of fatty acids are most frequently found. They form long needles (*a*), sometimes free and sometimes grouped together in rosets. They may be distinctly bent, and so perhaps may be mistaken for elastic fibers; but may be readily distinguished by the fact that they dissolve in potassium hydroxid or ether; or gently warming the preparation will melt the fat crystals and form drops of fat. Crystals of cholesterin (*b*), of leucin and tyrosin (*c*), are very rarely observed. They are formed chiefly in stagnating, putrid sputum. (See the figures on p. 605 et seq. for the identification of leucin and tyrosin.) Crystals of triple phosphate and of calcium oxalate (see Figs. 256, 257, and Fig. 254, p. 673) may be found in the sputum

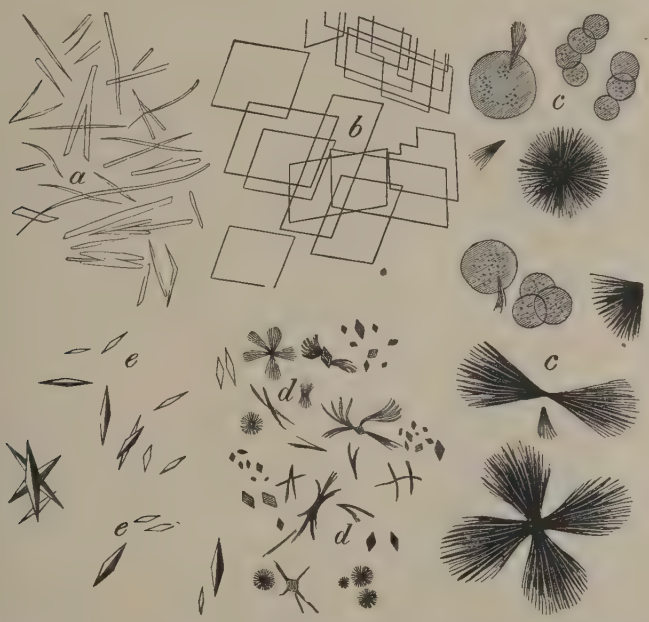


Fig. 278.—Crystals in the sputum: *a*, Fat; *b*, cholesterin; *c*, *c*, leucin (balls) and tyrosin (needles); *d*, *d*, hematoidin (bilirubin) in rhomboids and needles; *e*, *e*, Charcot-Leyden crystals.

under similar conditions. Hematoidin crystals (Fig. 278, *d*) are found chiefly in the sputum of abscess and of perforating empyema. The blood-pigment in pulmonary hemorrhages is mostly changed in the interior of the cells to amorphous pigment (see Heart-failure Cells), and but very rarely forms hematoidin crystals. Charcot-Leyden crystals (*e*) sometimes occur in the sputum. They are colorless, elongated, double pyramids, and vary considerably in size. They also occur elsewhere in the body during life and postmortem (in tumors, in stools, in leukemic blood, in bone-marrow, and in the spleen). They are very brittle, and, therefore, frequently observed with their ends broken off. They are soluble in hot water, mineral acids, and alkalis, and are stained by eosin.

Fr. Müller and Gollasch discovered a peculiar relationship between Charcot's crystals and the presence of eosinophilic leukocytes in the sputum. According to Müller, often as much as 60 per cent. of the leukocytes in asthmatic sputum are eosinophiles. Curiously enough, these eosinophiles are generally mononuclear, as contrasted with the ordinary neutrophilic leukocytes of pus and the eosinophilic leukocytes of the blood. It therefore seems rational to assume that Charcot's crystals are products of the crystallization of eosinophilic cells. This assumption is supported by the fact that the crystals readily stain with eosin, and that they occur in leukemic blood. (See p. 833.) Nothing definite is yet known regarding the chemistry of Charcot's crystals. Schreiner demonstrated that the so-called "Böttcher's sperm crystals" could be obtained by drying spermatic fluid. They resemble Charcot's crystals in appearance, and are the phosphate of an organic base (spermin, Pöhl). Schreiner's idea that they are identical with Charcot's crystals is pretty generally accepted. But Cohn[1] claims that these crystals differ considerably crystallographically, and that they belong to a different system. Charcot's crystals, as shown by their transverse surfaces, belong to the hexagonal system. They are doubly refracting, like Böttcher's crystals, but, unlike the latter, have a hexagonal transverse section.

These crystals are chiefly, but not exclusively, found in the sputum in bronchial asthma, so that for some time they were regarded as the exciting cause of the attacks. The bronchial nerves were supposed to be irritated by the pointed crystals. The relation, however, is not constant enough to justify any such conclusion. Asthma frequently occurs without crystals, and crystals are often found in the sputum without asthma. It seems much more rational to assume that during the asthmatic paroxysm, an opportunity is furnished for the formation of the crystals from eosinophilic cells, owing to the stagnation of the secretion products of the bronchial mucous membrane. *Curschmann's spirals* are to be included among these same products. The fact that Charcot's crystals are found in asthmatic sputum chiefly after the expectoration has been interrupted for a considerable length of time would seem to favor this theory. When expectoration is free and abundant, the crystals are usually absent. Furthermore, Charcot's crystals are found very abundantly in the interior of Curschmann's spirals; and, when the latter are preserved in a moist chamber, crystals may form in spirals which were previously free from them.

Animal parasites, or fragments of them, are very rarely found in the sputum. Amebæ (Amœbæ pulmonalis), flagellata (Trichomonas pulmonalis), and infusoria are very uncommon in the sputa, and of little importance clinically. They have been found in the sputum of pulmonary tuberculosis and of other pulmonary affections with cavities, as well as in Dittrich's plugs. (See p. 701.) Hooks, scolices, and bits of membrane of echinococcus may be found in the sputum in the rare cases where echinococcic cysts of the lung or liver perforate the bronchi. There is a disease in eastern Asia (Japan, China, Korea) which usually manifests itself by the occurrence of hemoptysis. It is due to the presence of a worm (Distomum pulmonale, recently named Paragonimus Westermanii[2]) in the lungs. Its eggs (Fig. 279) can always (often in great abundance) be demonstrated in the expectoration. They are oval, of a brownish-red color, 0.08 mm. long and 0.056 mm. broad, and are surrounded by a cuticle. They are easily identified under the microscope. They also occur in animals.

Fig. 279.—Distomum pulmonale with embryo (× 225) (after Nakahama-Leuckart).

Vegetable parasites are of greater interest and importance, especially the bacteria; the fungi play a more subordinate part. In

[1] Deut. Arch. f. klin. Med., 1895, vol. liv, p. 514.

[2] Inouye, Zeit. f. klin. Med., 1903, vol. l, p. 120. Stiles and Hassal, Sixteenth Report of the Bureau of Animal Industry, 1899.

examining the sputum for vegetable organisms, we should always bear in mind that by far the majority are saprophytic in nature, *i. e.*, they develop in the sputum either outside of the body, or, if within the air-passages, only in the secretion, and exist there in a more or less harmless way. To determine whether vegetable organisms in doubtful cases are expectorated as such, or are due to contamination of the sputum outside the body, we should examine the sputum fresh immediately after it has been expectorated. There are, however, a number of bacteria which can be distinguished with so much certainty from accidental contaminations that their presence, even in an old sputum, is of diagnostic importance. This is especially true of tubercle bacilli and pneumococci.

In obtaining sputum for bacteriologic examination a number of precautions must be observed. Since it is usually desired to examine the secretion originating in the deeper parts of the respiratory tract rather than that coming from the mouth, the mucopurulent masses should be selected instead of the thin secretion, which largely consists of saliva. It is well to examine only such clumps as are expectorated in the presence of the physician. If this be done, it is easy to determine from the character of the expectoration whether the mass has originated in the bronchi, in the larynx, in the pharynx, or in the nose. In order to reduce bacterial contamination from the mouth to a minimum, the oral cavity should be thoroughly washed with water just before the expectoration. The sputum obtained after this precaution is received in a clean glass; if cultures are to be made, the glass receptacle should be sterile and provided with a lid, so that the sputum may be immediately covered.

DEMONSTRATION OF TUBERCLE BACILLI IN THE SPUTUM

Tubercle bacilli are often so numerous in the sputum that they may be found with ease in any particle examined (Fig. 280); but in cases which are doubtful clinically and where the diagnosis depends entirely upon the examination of the sputum, tubercle bacilli may be found only after prolonged search. If the sputum be absolutely homogeneous, we must prepare a large number of slides without any particular selection. If mucopurulent, we can save time by spreading the expectoration upon a black background, and then selecting for examination the larger purulent clumps and any very cloudy, friable, cheesy-looking particles. Tubercle bacilli are also found even in slightly turbid or pure glassy sputum, although much less frequently. Tubercle bacilli may be found in the initial hemoptysis, although the patient seemed perfectly healthy beforehand. It is, of course, advisable in such a case to select particles which are not pure blood, but which have a certain amount of mucous and purulent material admixed. In a fresh hemor-

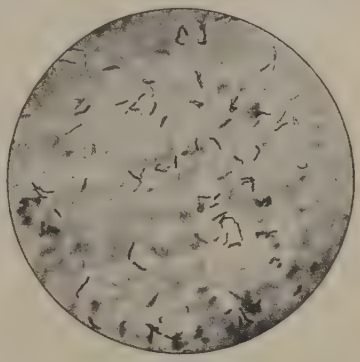


Fig. 280.—Tubercle bacilli (after a photograph by Günther) (× 500).

rhage from the lung, the more profuse the bleeding, the less chance of finding bacilli.

The recognition of the tubercle bacillus depends upon a special procedure by which they alone are stained. If unstained, they cannot be distinguished from other bacteria. The ordinary methods of staining bacteria are not suitable. A specimen is prepared by teasing a portion of the sputum to be examined, placing a small fragment of it or of the sediment (provided centrifugalization has been performed, see p. 713) upon a cover-slip, and then carefully spreading it. To obtain a uniform distribution, a second cover-slip is placed over the first, and the two then drawn apart with the fingers or forceps. Unless too much material has been used, a thin layer will be left upon each cover-slip, and this may be dried over an alcohol or gas-flame with a moderate degree of heat. Sputum may also be spread upon glass slides. It must then be *fixed* so that it will not wash off in the staining fluid. This is done by passing the slip rapidly through a flame three times. The principle of the special stain for tubercle bacilli depends upon the fact that these bacteria do not stain readily with the ordinary anilin colors, but that when they are once stained, they do not readily decolorize, even after the action of the strongly decolorizing mineral acids. An anilin dye which acts very intensely is selected; and for this purpose the ordinary basic anilin colors are the best, such as fuchsin or gentian violet, mixed with carbolic acid or with anilin. The directions for preparing this stain are given below. (See p. 711.) A few drops of the stain are dropped upon the cover-glass, and the latter held over the flame with a pair of forceps until the fluid steams. This process will stain the tubercle bacilli and all other organisms present.

The next step is to decolorize all the other organisms and any other morphologic constituents of the preparation. This is easily accomplished, because the tubercle bacillus holds the anilin colors with great tenacity. It is "acid-fast."[1] Some mineral acid is generally employed for decolorizing, most frequently nitric acid in some dilution or other, as mentioned below. The acid is allowed to work until the specimen appears entirely decolorized. This occupies a few seconds to a minute, according to the thickness of the preparation. If parts of specimens be too thick, we select only the thin places for examination.

After decolorizing, the preparation is washed in water. If any color remain, the acid must be renewed. It is sometimes necessary to alternate these two processes several times. The specimen is then mounted upon a slide with water or balsam, and examined with an oil-immersion lens and an Abbé condenser.[2] A much larger specimen can be prepared and examined directly with the oil-immersion lens by dropping some cedar oil upon the slide. Although this method is a very good one,

[1] See p. 712 in regard to the occurrence of tubercle bacilli which are not acid-fast.

[2] In balsam preparations the tubercle bacilli, as also other bacteria, almost always become decolorized in time, and in order to obtain a truly permanent preparation the author recommends that the stained smear be examined in water, after which it may be preserved by letting the water evaporate.

One edge of the cover-glass can be fastened to a slide with a drop of melted, hard, Venetian turpentine or colophonium, removed from the hard resin by means of a hot iron wire, or even with shellac. In the German clinics this method of dry preservation is considered the best for bacterial preparations as well as stained blood-smears.

it is not to be recommended, on account of the danger of scratching the objective by particles of mineral matter contained in the sputum. Such a dry preparation may be made upon the slide, but it should be covered by one large or several cover-glasses of the usual dimensions.

A counterstain after decolorizing aids in recognizing other micro-organisms or tissues in the specimen, and makes them form a contrast to the tubercle bacilli. Methylene-blue is well adapted for this purpose if the tubercle bacilli have been stained red. If gentian violet has been employed, Bismarck-brown and fuchsin are suitable counterstains. This second staining may be accomplished without heating. The counterstain should not be intense enough to obscure the tubercle bacilli.

Details in reference to the counting of tubercle bacilli will not be given, since the author can impute neither a diagnostic nor a prognostic value to such a procedure. The number of tubercle bacilli in a single preparation is dependent upon chance in the selection of the particle examined; and even when such chance is eliminated by the study of a large number of specimens, the prognosis and the gravity of the case are entirely independent of the number of tubercle bacilli in the sputum. For this reason he regards Gaffky's scale for the quantitative designation of the bacilli as valueless, and employs simply the terms "a few," "many," or "very many" tubercle bacilli.

Tubercle bacilli (Fig. 280, p. 709) are 1.3 to 3.5 μ long and 0.2 μ thick. They may, however, be 11 μ long. They are usually somewhat bent, often very markedly so. According to the method of preparation, they appear evenly stained, or, as a result of unequal distribution of the chromatin, beaded, consisting of stronger and weaker or unstained kernels ("streptothrix forms"). At times they form little clumps, in which the separate individuals lie criss-cross or parallel to one another. At times there are masses like an ear of corn or a brush. In certain cases, instead of the usual form, the "splitter" forms described by C. Spengler are found: kernel-shaped masses which betray their relationship to the tubercle bacillus only by the characteristic stain, and which have their analogy in the "splitter and kernel" forms of the non-acid-fast tubercle bacilli. (For the latter, see p. 712.)

Solutions for Staining Tubercle Bacilli.—1. A solution of fuchsin or gentian violet in saturated anilin water (Ehrlich). The latter is prepared as follows: 5 cc. anilin and 5 cc. absolute alcohol are mixed with 90 cc. distilled water, and if cloudy, filtered. The stain is prepared by adding 11 cc. concentrated alcoholic solution of gentian violet to 100 cc. of this anilin water.

2. A solution of fuchsin or gentian violet in carbolic water (Ziehl-Neelsen). One gram of fuchsin or gentian violet is mixed with 10 cc. of absolute alcohol and 100 cc. of a 5 per cent. solution of carbolic acid; or a saturated solution of fuchsin or gentian violet may be dropped into a 5 per cent. solution of carbolic acid until saturation takes place (formation of metallic sheen on the surface). These carbolic solutions have the advantage of keeping for a considerable length of time.

3. Czaplewsky[1] recommends the use of the following solution: One gram of fuchsin in 5 cc. acidum carbolicum liquefactum in a dish. Fifty cubic centimeters of glycerin are added, stirring constantly, and then diluted with 100 cc. of water. This solution keeps extremely well and does not need to be filtered.

Ordinary aqueous solutions without anilin or carbolic acid may be used (concentrated alcoholic stain dropped into water and prepared fresh each time). The stain is somewhat less intense. The other mixtures are preferable for diagnostic purposes.

[1] Hyg. Rundschau, 1896, No. 21.

4. The best decolorizing method is that of Czaplewsky, who employs Ebner's fluid, consisting of:

℞. Acidi hydrochlorici,
Sodii chloridi ..... āā 2.5
Aquæ destillatæ 100.0
Alcoholis 500.0

Before the employment of this fluid the specimen is washed with water; the decolorization may be accelerated by treating the specimen alternately with Ebner's fluid and water. The advantage of this fluid is that the other acid-fast bacilli are decolorized by the contained alcohol and cannot be confused with tubercle bacilli, as was the case with the purely aqueous solutions of acids previously employed.

Gabbet's method of decolorizing and counterstaining simultaneously, which was formerly almost universally employed, is not to be recommended, since Gabbet's solution contains no alcohol, and consequently will not guard against the confusion above mentioned.

As, apparently, individual tubercle bacilli may be decolorized by a too intense acid reaction, one oftentimes has to use milder decolorizing methods. In such cases Koch's original method of staining will serve the purpose. This consists in staining the tubercle bacillus with alkaline methylene-blue, decolorizing and counterstaining the other elements with a concentrated watery solution of Bismarck-brown. The method of Grethe described for the urine depends on a similar principle (see p. 694), where, after staining with carbol-fuchsin, the decolorizing and counterstaining are accomplished by an acid-free concentrated alcoholic solution of methylene-blue.

As a still milder decolorizing method, one may use 2 per cent. lactic acid, or, according to Kühne, 2 per cent. hydrochloric acid-anilin[1] solutions. In the latter case, the preparation, stained with the Ziehl-Neelsen solution, is placed for a few seconds in a 2 per cent. solution of hydrochloric acid-anilin and then decolorized in alcohol. This method is recommended when one wishes to demonstrate, together with the tubercle bacilli, the cellular elements, generally but little regarded.

Although the question of the staining of tubercle bacilli was presumably concluded long ago, M. Hermann[2] has recently recommended with especial emphasis a method little used, as a rule, but for a long time found by him to be trustworthy. To it is attributed the advantages of rendering at times the determination of tubercle bacilli possible when other methods fail, and of showing entire and intact bacilli when other methods stain only granules or "splitters." Hermann's stain consists of two solutions, to be kept separately -a 1 per cent. solution of ammonium carbonate in distilled water, which serves as a corrosive, and a 3 per cent. solution of crystal violet or methyl-violet (6 B) in 90 per cent. alcohol. Three parts of the first (the corrosive) are mixed with one part of the second (crystal violet solution). The stain should be left on the smear for one minute, while the slide is warmed over a flame until steaming begins. Decolorize with 10 per cent. nitric acid in 95 per cent. ethyl alcohol.

This method is particularly good for sections, especially for the determination of tubercle bacilli in lymph-glands of inoculated guinea-pigs. For this purpose the sections are carefully spread out on the slide, let dry, stained just as the dry preparations, then dried on the water-bath, and, without the use of xylol, are mounted directly in Canada balsam.

ON THE OCCURRENCE AND DETERMINATION OF THE NON-ACID-FAST TUBERCLE BACILLI, WHICH ARE NOT DEMONSTRABLE BY THE ORDINARY STAINING METHODS

The noteworthy fact that occasionally, in exceptionally destructive cases of pulmonary tuberculosis, no tubercle bacilli can be found in the sputum, is explained in part, according to H. Much,[3] by the fact that, together with the forms demonstrable

[1] See Borrel, Experimental Pulmonary Tuberculosis, Ann. de l'Inst. Pasteur, 1889, vii, p. 593.
[2] Ibid., 1908, No. 1, p. 921.
[3] Berlin. klin. Woch., 1908, vol. xiv, p. 691.

by the ordinary old method (decolorizing with acid), there exist forms which resist this method of examination, but which can be determined by Gram's method. (See p. 715.) These forms, according to Much, are: (1) Gram positive, small, non-acid-fast rods, generally granular, and (2) granular masses which morphologically correspond to C. Spengler's "splitter" forms, but, unlike these, are non-acid-fast and Gram positive.

This writer determined the genetic relationship of these abnormal forms to the ordinary tubercle bacillus by transforming the one into the other, and, at the same time, by demonstrating the virulence of the unusual variety. From this it may be concluded that it is important to employ the Gram method where the ordinary methods of examinations of the sputum show no tubercle bacilli. As the usual varieties of the tubercle bacillus are also stained by Gram's, the most rational method would seem to be to examine each case first for tubercle bacilli by Gram's method, and, if this be positive, to decide by a second preparation whether or not one is dealing with the ordinary acid-fast variety.

THE DIFFERENTIATION OF TUBERCLE BACILLI FROM OTHER ACID-FAST BACILLI IN THE SPUTUM

Occurrence of Smegma Bacilli in the Sputum

Pappenheim,[1] in Lichtheim's clinic, found smegma or nearly related bacilli in a non-tuberculous affection of the lung. They closely resemble tubercle bacilli in their affinity for acid stains. Laab found similar bacilli on the tonsils, on the tongue, and in the coating about the teeth. They are so rare, however, that probably very few serious mistakes have occurred. In examining urine for tubercle bacilli these smegma bacilli are of considerable importance. To avoid any mistake, Pappenheim's method of staining should be employed. This colors the tubercle bacilli red and the smegma bacilli and related forms blue. Pappenheim recommends the following procedure: (1) Stain in carbol fuchsin, heat to boiling-point for a few moments; (2) pour off the excess of carbol-fuchsin; (3) decolorize and counterstain, without washing, with the following solution, pouring it slowly three to five times over the preparation and allowing it to run off: One part of corallin is dissolved in 100 parts of absolute alcohol, and methylene-blue added until saturation (a considerable amount is necessary for this purpose); 20 parts of glycerin are then added; (4) wash quickly with water, dry, and mount. Duration of entire procedure, three minutes.

Confusion may be avoided by decolorizing the specimen stained in carbol-fuchsin with Ebner's fluid, as described above; or with Grethe's method (see p. 694), in which decolorization and counterstaining are accomplished by an alcoholic solution of methylene-blue and without any acid.

SEDIMENTATION OF TUBERCLE BACILLI

If the tubercle bacilli in a specimen of sputum be scarce, the examination may be facilitated by diluting the sputum and then centrifuging the mixture. This can best be accomplished as recommended by Biedert-Czaplewsky. One to 2 cc. of sputum are placed in a test-tube with six to eight times as much 0.2 per cent. solution of sodium hydroxid, shaken immediately, and then boiled once. After cooling, a few drops of a 1 per cent. alcoholic phenolphthalein solution, which colors the watery fluid a dark red, is added, 10 per cent. acetic acid is then added, drop by drop, until the color disappears. The fluid, if watery enough, is then centrifuged or allowed to settle; if not thin enough, it is first diluted with water. The resulting flocculent residue is used for making a dry preparation after first adding some of the original sputum, so as to make the layer stick, though this is rarely necessary. To determine the other micro-organisms which may be contained in the sputum, an antseptic, for instance, an equal volume of a 1 per cent. solution of carbolic acid, should be added, so as to prevent the growth of contaminating bacteria during the time consumed in settling if this method be adopted. Tubercle bacilli and other bacteria in the dilute sodium hydroxid above mentioned survive, and the tubercle bacilli will often be found, where they would be missed in the ordinary dry preparation.

Spengler's[2] method of making the sputum homogeneous by pancreatic digestion or by peptic digestion in acid solution so as to prevent decomposition, has

[1] Berlin. klin. Woch., 1898, No. 37, p. 809.
[2] Zeit. f. Hyg., 1894, vol. xviii, part 2.

no particular advantage over Biedert's original method, according to the data the author has been able to collect.

Ilkewitsch[1] recommends another method which is very useful for collecting tubercle bacilli in the sediment. This consists in stirring the sputum for some time with twenty times as much water, precipitating with acetic acid (mucin, nucleo-albumin), and then centrifuging.

THE DEMONSTRATION OF VERY FEW TUBERCLE BACILLI IN THE SPUTUM. IMPROVEMENT IN METHOD OF SEDIMENTATION (See Appendix.)

Despite all the perfections in the technic for demonstrating tubercle bacilli in sputum, frequently, as is well known, they cannot be discovered even in cases of perfectly evident tuberculosis. Hence, Ellerman and Erlandsen, of Copenhagen,[2] began to study the physical factors influencing the various sedimentation tests referred to above. They found that most of the difficulties encountered arose chiefly because tubercle bacilli of very light specific gravity are not readily centrifuged from so viscid a fluid as sputum, but that these difficulties can be partially overcome by diluting the fluid in two stages, being careful, in the former, to obtain a sediment which includes the bacilli concentrated in a smaller volume. These principles were recognized and employed by Ilkewitsch. (See above.) The sediment of the first dilution, comparatively rich in bacilli, is again diluted and centrifuged. They present a series of experiments which show that their so-called double method is much more reliable than any of the previously described sedimentation methods. In the first step, the authors make use of autodigestion at incubator temperature, with the addition of Na_2CO_3 solution, but not of trypsin. As a sediment forms the liquid becomes very thin. The resulting sediment is now allowed to settle, then dissolved in a solution of caustic soda (as in the Biedert-Czaplewsky test, see p. 713), the solution centrifuged, and from its sediment the slide prepared. They obtain a positive result from twenty to thirty times more frequently by this method than with simple dry preparations. The particulars of the technic follow:

(1) One volume of sputum (10 to 15 cm.) is mixed with one-half volume 0.6 per cent. Na_2CO_3 solution in a stoppered measuring glass, and is kept at 37° C. in a thermostat for twenty-four hours.

(2) Most of the superficial liquid is decanted, and the rest centrifuged in a graduated centrifuge tube. The supernatant liquid is then poured off.

(3) Four volumes of 0.25 per cent. NaOH solution are now added to one volume of sediment, the mixture then carefully boiled and stirred.

(4) The boiled fluid is centrifuged and the preparation made from the sediment.

[The so-called "enrichment method" of treatment with antiformin promises to be of considerable value in examining sputa containing only few bacilli. It has been found[3] that antiformin, which is a mixture of liquor potassæ chloratæ (Javelle water), one part, and sodium hydoxide solution, one and one-half parts, destroys all bacteria except the acid-fast varieties. The technic proposed[4] is as follows: Mix the sputum with sufficient antiformin to obtain 25 per cent. of the reagent in the resulting solution; stand for twenty-four hours; pour off the supernatant fluid and examine the sediment for bacilli in the usual way.—Ed.]

EMPLOYMENT OF ANIMAL EXPERIMENTS FOR DEMONSTRATING TUBERCLE BACILLI IN SPUTUM[5]

When no tubercle bacilli can be found in the sputum microscopically, even after sedimenting, animal experiments may be resorted to for diagnostic purposes. They may also be employed in attempting to distinguish the tubercle bacilli from other acid-fast bacilli. A suggestive portion is washed repeatedly and rubbed up in normal saline solution, and 0.5 to 1.5 cc. of the fluid injected into the peritoneal cavity or the groin of a guinea-pig. The weight of the animal is recorded, and it is killed in four to six or ten weeks, according to the diminution in its weight. An examination is then made to ascertain whether tuberculosis of the abdominal organs has developed. Even after two or three weeks tubercle bacilli can be often demonstrated in the pus expressed from a tiny fistulous tract originating in a swollen

[1] Baumgarten's Jahresbericht, 1892, vol. viii, p. 664.

[2] Zeit. f. Hyg., vol. lxi, No. 2, p. 219.

[3] Uhlenhuth, Centralbl. f. Bacteriologie, Abteill, vol. xlii, Beilage p. 62.

[4] Meyer, Zum Nachweiss von Tuberkelbazillocin Sputum mittels Antiformin, and Hune, Deut. med. Woch., 1909, vol. xxxv, No. 41.

[5] See Levy and H. Bruno, Deut. med. Woch., 1900, No. 9, p. 141.

and purulent lymph-node or from an ulcer at the point of inoculation or from an extirpated lymph-gland itself. Since the pseudotubercle bacillus produces similar lesions, it is necessary to prove that the organisms found are acid-fast. Sometimes the animals die in twenty-four to seventy-two hours, from an infection with pneumococci or streptococci. The experiment should then be repeated, after heating the sputum for ten minutes at 60° C., a temperature which will, according to the investigations of Forster and his pupils, kill all inflammatory organisms but not the tubercle bacilli.

To hasten the diagnosis of tuberculosis Bloch[4] has recommended that injections be made subcutaneously into the guinea-pig's groin and that the inguinal glands be then squeezed firmly between the fingers. Tuberculosis in these glands should be demonstrable both macroscopically and microscopically in from nine to eleven days. For staining sections, Hermann's method (see p. 712) should be considered.

THE DEMONSTRATION OF OTHER MICRO-ORGANISMS IN THE SPUTUM

For the determination of micro-organisms in the sputum the direct microscopic examination of the fresh sputum, expectorated just previously in the presence of the observer, has a much greater value than the much overrated culture method. (See later, Examination of the Mouth and Pharynx, Diphtheria Bacillus.) Most pathogenic bacteria present in the sputum occur in small numbers from time to time, in the mouths of healthy individuals as perfectly harmless occupants, so that the culture can deceive by distorting the relative proportions of the bacteria present, and, on the other hand, many pathogenic organisms are not easily grown from sputum without further measures.

They may be demonstrated in dry preparations made very much in the same way as those for tubercle bacilli, stained with the same solutions and according to the same methods, except that the subsequent treating with the acid is omitted. After staining, the preparations are washed in water only. If the stain be then too intense,the preparation may be subjected for a very few moments to the action of alcohol. The latter will remove any of the precipitated stain and render the bacteria more distinctly visible. Most bacteria possess so great an affinity for fuchsin, gentian violet, and methylene-blue that heating is unnecessary. Cold preparations will stain bacteria sufficiently inside of a few seconds to a minute.

Gram's Method.—Some bacteria stain very intensely with Gram's method, while the other elements of the sputum are decolorized. A dried specimen is stained with anilin gentian violet and then washed with water; Lugol's solution[1] is then added drop by drop. The iodin solution is allowed to act upon the preparation from one to three minutes; it is then washed with absolute alcohol until entirely decolorized macroscopically. When no further color can be washed away, the specimen is dried, and then examined in cedar oil or xylol balsam. The nuclei and the body of the preparation will appear entirely decolorized or very slightly yellow, but the micro-organisms will be stained intensely blue or almost black. By subsequent counterstaining (Bismarck-brown or fuchsin ten times diluted, Ziehl-Neelsen's or Czaplewsky's solution) a capital contrast stain is obtained.

Beautiful specimens may also be obtained, according to Czaplewsky, if Weigert's modification of Gram's method be combined with a fuchsin counterstain. Czaplewsky

[1] Berlin. klin. Woch., 1907, No. 17.

[2] This solution consists of 1 part of iodin, 2 parts of potassic iodid, and 300 parts of water.

describes the procedure as follows: Stain for one minute in carbolic gentian violet (11 cc. of a concentrated alcoholic solution of gentian violet, 10 cc. of alcohol, 50 cc. of a 5 per cent. solution of carbolic acid, 50 cc. of distilled water); wash thirty to sixty seconds. Lugol's solution (iodin 1, potassium iodid 3, water 200); wash, dry, differentiate with anilin-xylol 2 in 10, to which has been added 1.5 per cent. of acetone; wash with xylol, dry, restain with carbol-fuchsin diluted up to 1 in 10 (see p. 711) for about one minute, during which time the specimen is warmed slightly. The specimen is then washed, dried, embedded in Canada balsam, and examined with the oil-immersion lens.

Staphylococci, streptococci, diphtheria bacilli, tubercle bacilli (if stained with heat), anthrax bacilli, bacilli of tetanus, and Fränkel's pneumococci stain with Gram's stain (Gram-positive bacteria); whereas typhoid, colon, influenza, and cholera bacilli, Friedländer's bacilli of pneumonia, plague, glanders, and the pertussis bacilli decolorize with Gram's stain (Gram-negative bacteria).

This property of decolorizing is only a relative one, for individuals of certain species, which, as a rule, are not stained by Gram's stain, may retain their stain, and vice versâ. A great deal depends upon the intensity of action of the decolorization. Where mixtures of bacteria and not pure cultures are being treated, as in the examination of sputa, the question whether certain bacteria decolorize after Gram's stain can best be decided by subsequently counterstaining with a fuchsin solution diluted ten times. Bacteria which decolorize after Gram's stain will then be stained red, and the Gram-positive bacteria blue to black.

The demonstration of *Fränkel's pneumococci* in the sputum is of considerable diagnostic importance. They are usually elongated, lance-shaped cocci, generally arranged in pairs with their bases approximated. They are surrounded by a faintly staining capsule, which in dry preparations usually does not stain at all. Fränkel's pneumococci have been shown to be the cause of croupous pneumonia. They must not be confounded with other diplococci found in the sputum, more especially with Friedländer's[1] so-called diplococci. The latter also possess a capsule, but they have nothing to do with the etiology of croupous pneumonia, although they may sometimes be present with pneumonia. Friedländer's cocci, when strongly magnified, are seen to be short, plump bacilli much larger than pneumococci. Cultural differences also exist, and Gram's stain decolorizes them, but stains Fränkel's diplococci. W. Wolf has furnished us with a very useful double stain for Fränkel's diplococci. The dry preparation is first of all stained in anilin water saturated with fuchsin, and then placed one to two minutes in a diluted, transparent aqueous solution of methylene-blue. The cocci stain blue, the capsule rose color, and the body of the preparation a bluish red. [Staining with India ink brings out the capsule very plainly.—Ed.]

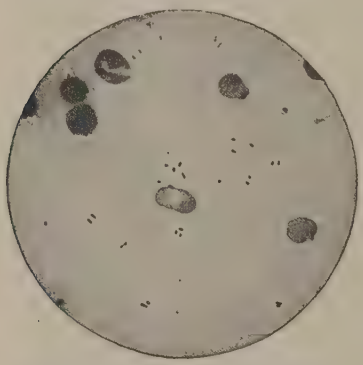


Fig. 281.—Fränkel's pneumococci (from a photograph by Fränkel) (× about 800).

[1] [Friedländer's micro-organism is a species of bacillus belonging to the same group as the various species designated Bacillus mucosus capsulatus.—Ed.]

The diagnostic significance of pneumococci is limited, because the same organism may be found in the normal secretions of the mouth and in non-pneumonic sputum. It is identical with the organism of an experimental sputum septicemia of rabbits and mice. The pneumococci, however, are found in very small numbers in normal mouth secretions. According to modern views, any bacteria found in the body normally may, under certain conditions, acquire pathologic significance, so that we need not modify the etiologic importance of Fränkel's cocci in pneumonia.

In the saprophytic forms, the capsule formation, according to Kolle, is less pronounced than in the pathogenic.

Pneumococci are not always easily differentiated from streptococci, as they can grow in chains in excretions as well as in culture, and the pneumococcus and the streptococcus may both show lanceolate forms. The distinction is even more difficult, as the elongated form of the individual coccus, as well as the capsule, is not absolutely characteristic for the pneumococcus. They are frequently encountered among the ovoid-shaped streptococci, some with elongated form and vice versâ; there occur among pneumococci perfectly round or ovoid forms. All this apparently depends upon the intensity of the growth. And, further, there are streptococci with capsules, the Streptococcus mucosus. In culture also the differences are often not distinct.

According to Levy,[1] one differential point between the pneumococcus and the streptococcus is that the former is decomposed in bile, or rather in a solution of sodium taurocholate, in contradistinction to the streptococcus. If 0.1 cc. of rabbit's bile or of a 10 per cent. solution of sodium taurocholate be mixed with 0.5 cc. of a bouillon culture of pneumococcus, the cocci are decomposed in from three to twenty minutes, and the culture is then sterile. The Streptococcus mucosus, which is closely related to the pneumococcus (if it be not identical with it), is the only streptococcus which behaves under these circumstances just as the pneumococcus.

With reference to the differences of hemolytic action, see p. 720.

The *influenza bacillus*[2] was described by R. Pfeiffer as the cause of the great epidemic of influenza in the early part of the nineties. It is of some diagnostic importance (Fig. 782).

It is a very small bacillus; is hard to stain; is sometimes arranged in pairs; is always found in fresh attacks of true influenza, and usually in very great numbers, free or included in the leukocytes. In parts of the sputum it may be obtained practically in pure culture. Pfeiffer obtained the best-stained specimens by allowing dry preparations to float five or ten minutes on a very dilute, pale-red solution of carbol-fuchsin. Influenza bacilli are only two or three times as long as they are broad. They rarely form threads. The ends are rounded off, and with faint staining will be somewhat more deeply colored than the center, so that they may resemble a diplococcus. This appearance may also be produced if two short rods lie side by side. Influenza bacilli have no capsule and are not mobile. They do not stain by Gram's method. Influenza bacilli can be cultivated only on media containing hemoglobin, a fact which may serve to differentiate them, for instance, from the colon bacillus. An appropriate medium can be easily prepared by spreading a little blood with the infected material upon the surface of ordinary agar. In regard to the character of the colonies and the results of animal inoculations, we must refer to Pfeiffer's original work.

In late years, at least in Switzerland, the influenza bacillus has hardly ever been found in the so-called attacks of influenza. On the

[1] Virchow's Arch., 1907, vol. clxxxvii.
[2] Zeit. f. Hyg., 1893, xiii, p. 357 et seq.

contrary, the causative agent has apparently been the pneumococcus of Fränkel, for it has been found in the sputum of these cases frequently in great numbers, even when there were only signs of bronchitis and without pneumonia. If the influenza observed in the nineties be

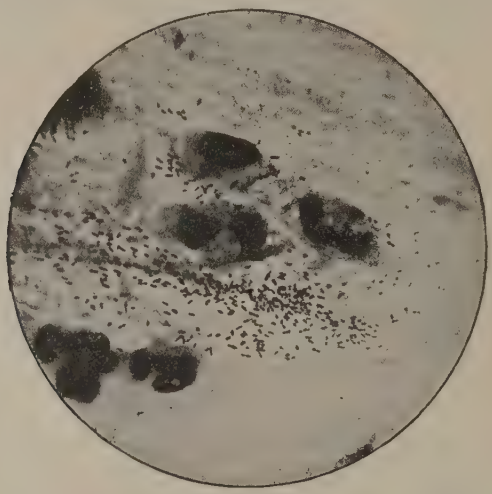


Fig. 282.—Influenza bacilli (× 1000) (after Pfeiffer).

regarded as a specific disease produced by the influenza bacillus, which does not seem to the author to have been absolutely established, it might be well to limit the term influenza to cases with the influenza

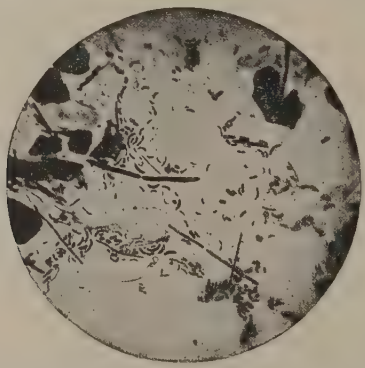


Fig. 283.—Saprophytic bacteria of the mouth, from the gums. The large rods are Leptothrix buccalis (× about 800) (after Fränkel).

bacillus, and to cease applying this name to pneumococcic infections and common catarrhal conditions.

Has it then become unfashionable to diagnose a coryza or a bronchitis, or, if one wishes to diagnose etiologically, a catarrhal coccus

(meningococcus) coryza, a pneumococcus bronchitis, pneumococcus tracheitis, or pneumococcus pharyngitis? Is catching cold dismissed as a cause of transient illness attended with fever? Who has dismissed it? With what right? Has it become a menace to one's reputation to diagnose such things, and is it scientific, according to the ideas of laymen, to allow the nebulous phantom of influenza suddenly to loom up on all sides? Is it right and necessary to console a tuberculous patient who has fever with the diagnosis of influenza, instead of with an explanation that his illness has proceeded to a febrile stage, and with the prediction that the fever will again disappear?

Leptothrix buccalis and *other saprophytic bacteria* are often observed in fresh sputum, for they grow in the normal mouth and there become mixed with the expectoration (Fig. 283). They may multiply in the lung under pathologic conditions and appear very abundantly in the sputum, especially in putrid diseases of the lung. They do not seem to have any actual pathogenic significance, except that they may play a

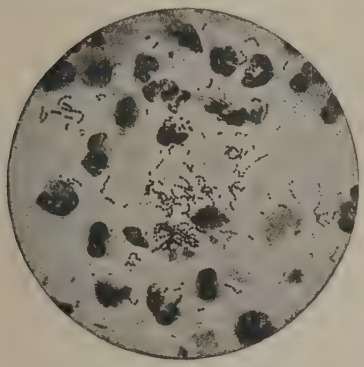


Fig. 284.—Streptococcus pyogenes (× about 800) (after Fränkel).

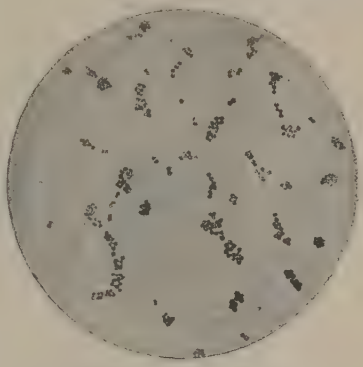


Fig. 285.—Staphylococcus pyogenes aureus (culture) (× 1000) (after Weichselbaum).

very considerable part in the putrid decomposition of secretions. The bacillus known as Leptothrix buccalis or pulmonalis may be easily recognized by its size and shape and its peculiarity of frequently (not always) staining blue with Lugol's solution. This latter peculiarity seems to depend upon the starch content of the nutrient medium.

The *Micrococcus tetragenus* may be found in the sputum in various conditions: in bronchitis, in cavities of the lung especially, and sometimes in the saliva of healthy people. It is a Gram-positive organism. The tetrads are usually isolated, and often surrounded by a colorless or faintly stained capsule. They can be distinguished from sarcina groups in being composed of one layer of four individual organisms, and not of a cube, like the sarcinæ(8). It is pathogenic for animals, white mice, and guinea-pigs, and may also produce suppuration in man. Very possibly it aids the tubercle bacillus in destroying the lung tissue in phthisis. It grows readily upon the ordinary nutrient media and does not liquefy gelatin.

The same possibility applies to the *streptococci* and *staphylococci*, which are (Fig. 284) found not infrequently in very great numbers in tuberculous sputum.

With regard to the differentiation of streptococcus and staphylococcus, it may be remarked that a distinction is not always possible in the secretions, because the streptococcus does not always form chains, and the staphylococcus can, under circumstances, also form isolated, generally short, chains of three or four individual

cocci. On the other hand, the differentiation by culture is always easy. (See the many text-books on Bacteriology.)

Pathogenic, *i. e.*, the virulent, streptococci generally form longer chains ("Streptococcus longus") than the avirulent. According to Mandelbaum,[1] the different varieties of streptococcus can be differentiated on blood agar (2 parts blood and 5 parts agar), since the markedly pathogenic forms ("Streptococcus longus") decolorize the media about them by their hemolytic action, while the less pathogenic "Streptococci mitior" ("S. viridans") and the "Streptococcus saprophyticus" do not do this. The author observes that the green coloration of the blood media attributed to the non-hemolyzing streptococci serves merely for contrast.

With reference to the distinction between pneumococci and streptococci see p. 717. On solid blood media the former behave as Streptococcus mitior, *i. e.*, they are non-hemolytic.

The *Micrococcus catarrhalis* is almost always found in the nasal secretion in rhinitis, and is quite frequently observed in the sputum from the lungs. It differs from the ordinary staphylococci by its much larger size, by its decolorization by Gram's method, and by its frequent intracellular location. With the exception of its larger size, it closely resembles the gonococcus, and, like the latter, as well as like the ordinary staphylococcus, is frequently grouped in pairs as a diplococcus, the contiguous sides of the paired cocci appearing distinctly concave.

More and more proof accumulates that the micrococcus is identical with the meningococcus intracellularis.

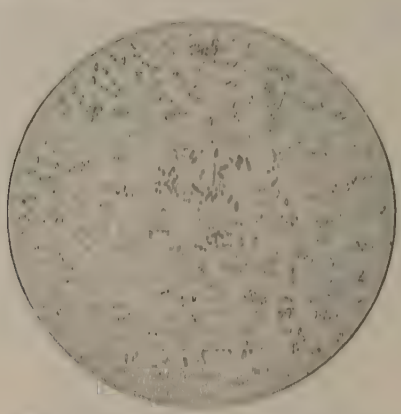


Fig. 286.—Bordet's bacillus of whooping-cough.

Bordet's Bacillus of Whooping-cough.—Bordet[2] found in the sputum of whooping-cough a specific bacillus, short, Gram negative, and colored more strongly on the ends (Fig. 286). He cultured it, and demonstrated by agglutination and complement deviation experiments that it was the specific cause of whooping-cough. These findings have been confirmed by Arnheim.[3] Cultures do not grow on ordinary nutrient media, but only on faintly acid media, poor in nutrient material, with a substratum of ascitic fluid or blood, which hinders the growth of most saprophytic and pus-forming organisms. Upon his culture media it grows at first very sparingly and almost invisibly and only abundantly by transplantation. The sputum of the early stage of the disease serves best for cultivation. Bordet prepares his media as follows: To 200 cc. of water, containing 4 per cent. of glycerin, is added 100 gm. of potato, cut in slices. This is cooked in an autoclave, the fluid decanted, and a glycerin-containing potato extract is thus obtained. Fifty cc. of this extract, 150 cc. of a 0.6 per cent. sodium chlorid solution, and 5 gm. of agar, are let digest in the autoclave. The fluid is filtered into test-tubes while still warm, 2 to 3 cc. to each tube, and then sterilized. Some blood from a guinea-pig, or better from the human,

[1] Zeit. f. Hyg., vol. lviii, part 1.
[2] Ann. Pasteur, 1906, No. 9, and 1907, No. 9.
[3] Berlin. klin. Woch., 1908, No. 31.

is obtained and defibrinated under aseptic precautions, and an equal amount of the defibrinated blood is added to the agar in each test-tube, shaken up, and the tubes are then placed on a slant and allowed to cool. This medium serves for the culture of other delicate micro-organisms besides the whooping-cough bacillus, such as the gonococcus, meningococcus, influenza bacillus, and others, which are easily overgrown by saprophytes on ordinary media.

In recent years bubonic plague has occasionally occurred in regions in which the disease is not endemic, and the *pest bacillus* must consequently be described. Although bacteriologic laboratories will usually make the bacteriologic diagnosis of bubonic plague, it will occasionally happen that the physician will be forced to make his own diagnosis, and in such cases he should be familiar with the method of bacteriologic examination. This is particularly necessary in the cases in which the lungs are affected, since the clinical course of the disease may then almost exactly correspond to that of an ordinary catarrhal or croupous pneumonia. Enormous quantities of pest bacilli may be found between the red blood-corpuscles in the hemorrhagic sputum of such cases. The pest bacilli may also be present in the expectoration in the ordinary bubonic plague. Czaplewsky describes them as follows: They are usually short rods with rounded ends, their length being two to three times greater than their breadth. They are occasionally so short, however, that they resemble cocci. They are readily stained, the poles appearing darker than the central portion, which may be pale or even colorless. (See Fig. 289.) This polar

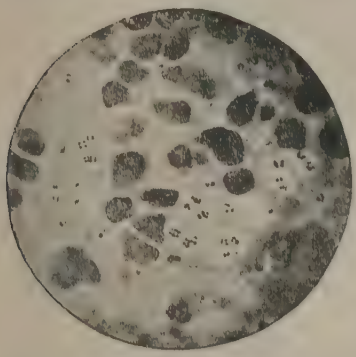


Fig. 287.—Micrococcus tetragenus (× about 800) (after Fränkel).

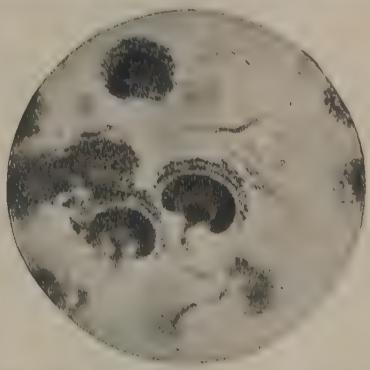


Fig. 288.—Aspergillus fumigatus (× about 350) (after Fränkel).

stain may be most beautifully obtained by staining the bacilli for a half-minute in dilute borax methylene blue (stock solution with 2 per cent. methylene blue and 5 per cent. borax). The pest bacilli are decolorized by Gram's method. They are non-motile. For methods of cultivation the reader is referred to the official communications of the German government for the bacteriologic diagnosis of bubonic plague (published by J. Springer, 1902), and to the works of Kossel and Overbeck (from the Imperial Health Office, 1901, Part 1).

In pulmonary glanders the *Bacilli mallei* may be found in the sputum. They cannot be sufficiently identified by microscopic examination, but for identification require to be grown in cultures, and particularly to be inoculated into the lower animals. They are of about the same length as tubercle bacilli, but are thicker and have rounded ends. They are non-motile, and are decolorized by Gram's method. Particularly characteristic is an alkaline potato culture, which, after two days at a temperature of 37° C., presents slimy, drop-like colonies, varying in color from honey yellow to copper red, about which the potato is darkly stained. Kolle states that other bacteria, *e. g.*, Bacillus pyocyaneus, may exhibit a similar growth. Bacillus malleus grows upon most slightly alkaline nutrient media, and best between 33° and 37° C. Experiments upon animals are performed as follows: A guinea pig is inoculated subcutaneously with the suspected material. From the resulting swollen glands a tiny piece is excised and introduced into the peritoneal cavity of another male guinea pig. Upon the second or third day this second animal develops a characteristic orchitis produced by glanders. Since other bacteria may also pro-

duce an orchitis, the morphologic and cultural characteristics of the Bacillus mallei must also be taken into consideration.

In the so-called wool-sorters' disease, which is nothing else than pulmonary anthrax, the *Bacillus anthracis* may be found in the sputum. (See Fig. 309.) These bacilli are easily stained, and may be readily recognized by their size (length 5 to 10 μ, breadth 1 to 1.5 μ). The ends are frequently slightly concave, giving rise to the so-called bamboo form. They liquefy gelatin and grow out into long, waving chains, which develop endogenous, highly refractile spores. Mice quickly die after the subcutaneous inoculation of anthrax bacilli; the edematous fluid at the site of the inoculation and the blood contain large numbers of the bacilli.

The occurrence of *typhoid bacilli* in the sputum is of very slight diagnostic importance. It has been particularly observed in the pneumonia of typhoid fever. The author himself has seen a case of typhoid in which a serous pleuritic exudate containing large numbers of typhoid bacilli perforated into the respiratory passages and was expectorated.

The presence of *sarcinæ* in the sputum possesses a certain amount of interest They resemble and are often confounded with the Micrococcus tetragenus, but are considerably larger. (See p. 719.) They are very rarely found in the sputum. True sarcinæ are best seen in unstained preparations. Fig. 201, *c* and *d*, gives some idea of their appearance. It has not as yet been definitely settled whether or not the

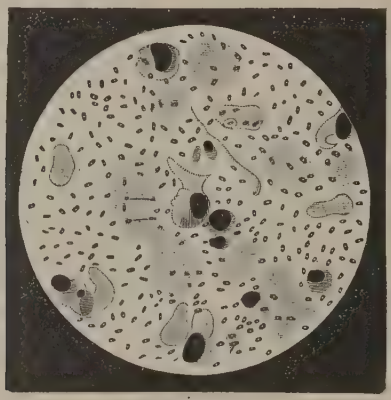


Fig. 289.—Pest bacilli in a smear made from a bubo; stained with methylene-blue (Kolle).

sarcinæ of the stomach (described above) are identical with those of the lung. Sarcinæ have been found in the sputum, chiefly in gangrene of the lung, but also in tuberculosis, bronchitis, and pneumonia (pneumonomycosis sarcinica). Sarcinæ should probably be considered saprophytic, especially when we consider their occurrence in all these conditions. The same type of sarcina may develop in the mucous membranes of the mouth and pharynx of debilitated patients, producing the grayish spots of pharyngo- or stomatomycosis, and from this source may be found in the expectoration.

Yeast fungus has also been observed in sputum, although in most cases it is an accidental contamination, yet, from a case recorded by Busse,[1] it is not to be denied that it can have pathogenic significance. In these cases there are moderately small yeast-cells, 8 μ in diameter, strongly refractile, becoming clearer on the addition of dilute soda solution.

It has recently been found that various kinds of molds belonging to the genus *Aspergillus* (Figs. 288 and 290), or perhaps to the genus *Mucor*, may develop in the lung; but practically only when there is some coexisting destructive cavity formation, with a few exceptions described by Saxer and others. The cavities where these molds have been found are almost exclusively devoid of odor. The relation of the molds to putrefactive bacteria observed outside of the body would seem to

[1] See Kolle and Wassermann, Handb. d. path. Microorg.

make it probable that the constant antagonism between these two kinds of organism continues in the interior of the body, so that the aspergilli protect a pulmonary cavity from putrefactive bacteria; and, conversely, the saprophytic bacilli found in the majority of cases protect the lung from becoming overgrown with some mold. Molds only very exceptionally invade an otherwise healthy lung; but if they once settle there, they aid in the general destruction, as is definitely proved by the examination of the pathologic processes. Very likely they may even displace the primary pathogenic bacilli. Cases where *pneumonomycosis aspergillina* or *mucorina* seems

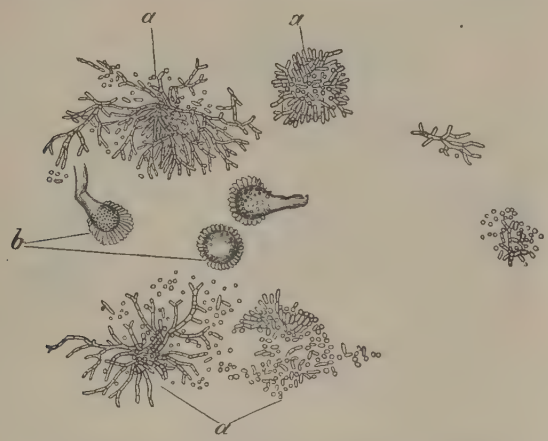


Fig. 290.—Aspergillus fumigatus of the lung (partly schematic): *a*, *a*, *a*, Mycelium of aspergillus in roset-like rays; *b*, sporangium (× 285) (after Weichselbaum).

to be primary can be explained in this way. It has not been proved that they ever occur primarily, and although the spores of aspergillus are everywhere, yet Aspergillus mycosis is extremely rare. The only diagnostic criterion differentiating pneumonomycosis aspergillina or mucorina from ordinary bronchitis, phthisis, etc., is the demonstration of the molds in a fresh specimen of sputum, or in a dry specimen stained with saffron or thionin (Figs. 288 and 290) (mycelium, spores, conidia). The varieties, as a rule, can be separated only by culture (sterile moist bread, see special text-books).

Fig. 291.—Oïdium albicans (× 400) (after Bizzozero).

Up to the present time there have been described, to the author's knowledge, only four cases of mucor mycosis of the lung,[1] all of which have to do with different species of mucor. More often there are aspergillus infections, in which the Aspergillus fumigatus is concerned. With regard to the clinical condition, the reader is referred to Sticker's article, "Mold Infections of the Lung," in Nothnagel's System, 1900.

In rare cases the *Oidium albicans*, another mold, may develop in the lung. It is best detected in fresh, unstained preparations of sputum (Fig. 291). It develops much more frequently upon the mucous membranes of the mouth, pharynx, and esophagus than in the lung. From any one of these sources it may be found in the sputum (Fig. 291). It shows best in unstained preparations.

[1] See Emerson, Clinical Diagnosis, 1906.

The rare cases of *actinomycosis*, the disease caused by *ray fungi*, which infect the human lung, should be mentioned. Their course clinically is similar to that of tuberculosis of the lung, except that instead of the tubercle bacillus, this fungus is found. The characteristic yellowish or grayish-green granules (the size of a poppy seed) of actinomycosis can generally, but not always, be recognized with the naked eye (Fig. 292). The microscopic examination is not always decisive either. In some cases the microscopic rosets of the fungus are to be found; in others only the branch-

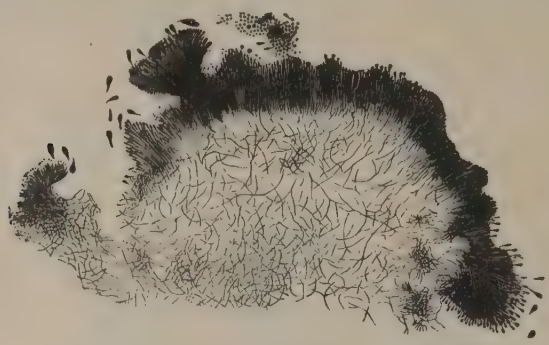


Fig. 292.—Young actinomyces granule (prepared section). In the middle, the mycelium; on the edge, the clubs, which become much thicker with maturity. From a preparation stained by Gram's method (× 530) (after Weichselbaum).

ing threads staining by Gram's method (Fig. 292), with or without club-like ends. Occasionally even coccus-like structures are found, the actinomyces belonging to the pleomorphic class of streptotriches. Generally speaking, microscopic elements of this sort make the diagnosis of actinomycosis very probable; still, it is wise to follow Silberschmidt's[1] advice, and prepare aërobic and anaërobic bouillon and agar cultures for the purpose of differentiation. This fungus grows anaërobically.[2]

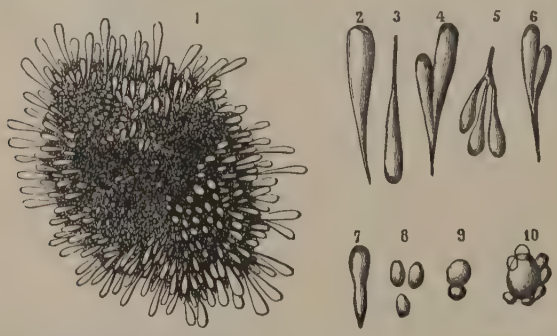


Fig. 293.—Actinomyces from a tumor of the lower jaw of a cow: 1, An entire granule (× 500); 2, 3, 4, 5, 6, 7, different forms of clubs; 8, 9, 10, round elements (× 1000) (after Mace).

Streptothrix of the lung is closely related to the last-named fungus, and in the sputum of an infected individual similar granules are to be found. The threads may branch and resemble those of actinomycosis; they are also Gram positive. Clubs rarely occur. It grows, however, aërobically.

[1] Zeit. f. Hyg. u. Infectionskrankh., 1901, vol. xxxvii, p. 345.

[2] [In this connection the reader is referred to J. H. Wright's exhaustive study, The Biology of the Micro-organism of Actinomycosis, Jour. Med. Research, Boston, 1904–05, xiii, p. 349.—Ed.]

CHEMICAL EXAMINATION OF THE SPUTUM

ALBUMIN IN THE SPUTUM

Wanner[1] calls attention to the diagnostic importance of the presence of albumin in the sputum. The greater the quantity of albumin in the expectoration, the more marked will be the inflammatory process to which the sputum owes its origin. From a practical standpoint, Wanner notes that the sputum of a simple chronic bronchitis is always practically free from albumin, while that of pulmonary tuberculosis is usually characterized by a distinct quantity of albumin.

To demonstrate this albumin, a measured quantity of the expectoration is placed in a glass flask with a 3 per cent. solution of acetic acid, and violently agitated until the mucus is decomposed. The mixture is filtered, and the residue is washed with 3 per cent. acetic acid. The strongly acid filtrate, which contains the albumoses and the albumin of the sputum without the mucin, is now treated with sodium hydroxid until it is only slightly acid in reaction. If necessary, concentrated saline solution may be added, after which the albumin may be coagulated by boiling. The albumin may also be precipitated from the strong acetic acid solution by potassium ferrocyanid. In either case the resulting precipitate gives a qualitative and a quantitative test for the amount of albumin in the sputum. Esbach's method, as applied to the urine (see p. 615 et seq.), may also be employed for an approximate quantitative estimation of the amount of albumin.

Wanner estimates the mucin content of the sputum from the glucosamin split off from the mucin by boiling with dilute acid. The sputum is first shaken up with two volumes of alcohol, filtered through hardened filter-paper, and washed with alcohol. The precipitate is then boiled for three hours with 10 per cent. HCl in a flask with a return condenser, cooled, neutralized to a very weak acid reaction, precipitated with phosphotungstic acid, in order to separate the biuret reacting bodies, and then with alkaline copper solution: the reducing action of glucosamin is estimated qualitatively and finally quantitatively. Glucosamin has nearly the same reducing power as glucose. Mucin contains 33.6 per cent. glucosamin.[2]

The color examination of sputum by means of stains should here be described. This procedure was inaugurated by A. Schmidt, who stained sputum with Biondi's triple stain. Zenoni's method is simpler. The sputum is spread in a thin smear on a cover-glass or slide, hardened in alcohol for at least a quarter of an hour, and stained with a half-saturated watery solution of safranin. When examined on a white background, the mucin is stained yellow and the albumin red.

CHIEF CHARACTERISTICS OF THE MOST IMPORTANT TYPES OF SPUTA

CATARRHAL OR BRONCHITIC SPUTUM

Ordinarily, catarrhal sputum is essentially mucopurulent without any other admixtures. In the beginning of an acute bronchial catarrh the mucus usually predominates and the sputum is scant. After a few days the expectoration becomes more abundant, less tenacious, and considerably more purulent, the general discomfort at the same time lessening. As recovery progresses, the amount of pus diminishes with the diminution in the quantity of expectoration, until the sputum disappears entirely. In chronic bronchitis the nature of the expectoration may vary considerably, being at times more, at times less, purulent. Patients usually feel more comfortable when the sputum is fairly abundant; whereas the discomfort is increased when the secretion becomes excessive or if it cease entirely.

[1] Deut. Arch. f. klin. Med., 1902, vol. lxxv, parts 3 and 4.
[2] See also the work of F. Müller, Zeit. f. Biol., vol. lii.

SPUTUM IN FIBRINOUS OR CROUPOUS BRONCHITIS

The sputum of croupous differs from that of ordinary bronchitis. Fibrinous coagula in the shape of casts of the bronchi appear in the sputum from time to time, usually associated with more or less blood. Charcot's crystals are very frequently found in these formations. The larger coagula are apt to be expectorated with very severe paroxysms of coughing, which have usually been preceded by more or less dyspnea. Hochhaus has shown that similar formations composed of mucus may occur in this affection.

SPUTUM IN ORDINARY PULMONARY TUBERCULOSIS

Macroscopically, this cannot be absolutely distinguished from simple catarrhal sputum. Any type may be present, from a purely mucous to an almost purely purulent sputum. In well-advanced ulcerative types of phthisis the amount of pus is usually considerable. Friable, opaque white particles always make one suspect tuberculosis. The sputum of tuberculous patients frequently has a very bad odor, especially if there be cavities with stagnating contents. A positive diagnosis of tuberculosis can be made only when the tubercle bacillus is found; but if all other destructive processes of the lung can be eliminated, elastic fibers are very suggestive. The abundance of these morphologic elements by no means indicates the severity of the case. There are very severe cases of tuberculosis of the lungs where no bacilli and no elastic fibers can be found. These are frequently very malignant and acute cases, where the constitution is undermined before disintegration of the pulmonary infiltration begins, or cases where miliary tuberculosis is alone responsible for the grave symptoms. Again, if the catarrhal secretion be profuse, which is common, especially in unfavorable cases, the number of tubercle bacilli in the sputum will seem few on account of the dilution. On the other hand, we not uncommonly find tubercle bacilli and elastic fibers in the sputum of early tuberculosis of the lung, where physical examination reveals no abnormal signs or only slight ones. The significance of tubercle bacilli in cases of this sort is of very decided importance. Naturally, then, any variation in the number of elastic fibers or of tubercle bacilli which are present in the same individual cannot be interpreted, in and of itself, as indicating any marked change in the course of the disease. In judging the value of therapeutic measures, such false interpretations have frequently, although improperly, been applied.

SPUTUM IN ACUTE MILIARY TUBERCULOSIS

This presents the characteristics of an ordinary catarrhal sputum, and if not complicated by ulcerative phthisis, is without bacilli. There may be no sputum at all. (See p. 534 in regard to the occurrence of tubercle bacilli in the stools in this affection.)

SPUTUM IN CROUPOUS PNEUMONIA

The characteristic feature of the sputum of croupous pneumonia is its blood-content. The blood is usually uniformly mixed in a glairy menstruum, the sputum appearing almost transparent and homogeneous. Not infrequently, however, particles of sputum free from blood alternate with hemorrhagic streaks and spots or with considerable quantities of almost pure blood. In many cases the original color of the blood is almost completely preserved; in others, especially when the blood is uniformly mixed with the glairy menstruum, the blood pigment is modified to a yellowish or brownish red, as previously described (*rusty sputum, sputa crocea*). Blood-corpuscles can be recognized microscopically in any pneumonic sputum, although they are almost completely laked out. The peculiar change of blood-pigment producing green and yellow sputa has been already considered (p. 697). Pneumonia not infrequently gives rise to jaundice (p. 42), in which case the sputum is apt to be yellow or greenish and show Gmelin's reaction (p. 575). Fibrin coagula are not uncommonly found in the sputum of pneumonia; we have already considered (p. 702) their peculiarities and the method of demonstrating them. If the croupous pneumonia and the fibrinous bronchitis of the smaller bronchi, by which it is almost always accompanied, be complicated by a catarrhal bronchitis of the larger bronchi, then the purely pneumonic sputum will be mixed with catarrhal elements. Pneumonic sputum is usually very viscid, on account of the nuclein it contains so much so that the spit cup may be completely inverted without spilling the contents.

Thin, liquid sputum, especially if it be abundant and dark reddish brown in color, is often an unfavorable sign in pneumonia, as it frequently indicates the beginning of pulmonary edema. Such a dark sputum has been called "prune-juice" sputum, on account of its appearance. However, we should not make a prognosis from the nature of the sputum alone. A thin, liquid sputum is an unfavorable sign only when the other symptoms are very urgent, for not infrequently a liquid sputum indicates the beginning of resolution. Fränkel's pneumococcus can always be demonstrated in the sputum of croupous pneumonia (Fig. 281).

SPUTUM IN BRONCHOPNEUMONIA

We include here deglutition and hypostatic pneumonias. In these disorders the sputum sometimes resembles bronchitic sputum or, like that of croupous pneumonia, it contains blood. This is easily understood, for it is frequently very difficult, aside from the macroscopic distribution, to distinguish broncho- from croupous pneumonia histologically, and, like the latter, bronchopneumonia may also be hemorrhagic, with a more or less fibrinous exudate. The bacteriology of bronchopneumonic sputum may vary considerably. Fränkel's pneumococci are not infrequently found, as well as many other pathogenic micro-organisms.

SPUTUM IN PULMONARY GANGRENE

This is characterized mainly by its intensely disagreeable odor. It is usually very abundant and liquid, and of a dark, dirty-greenish or brown color. Greenish-black particles of necrotic lung tissue can be found macroscopically in it, and besides them, constituents characteristic of hemorrhagic, pneumonic, catarrhal, or purulent sputum. Odorless gangrene is very uncommon. The author once demonstrated an abundance of sarcinæ in the necrotic portions from a case of this sort. If allowed to stand, the sputum of pulmonary gangrene usually separates to form layers, the uppermost layer containing mucus and necrotic portions, admixed with air, which float. The second layer is liquid, and, the third (the sediment) consists of pus-corpuscles and necrotic detritus. Besides the ordinary elements of sputum, abundant bacteria of decomposition, fatty crystals, cholesterin, leucin and tyrosin crystals (Fig. 278, *c*), pigment, and bits of destroyed lung tissue are seen microscopically. Elastic fibers may be absent.

SPUTUM IN PULMONARY ABSCESS

This is essentially a purulent sputum, and often has a very foul odor. A characteristic of the pus when mixed with water is its fine, shredded, flocculent appearance. (See p. 701.) If catarrh exist at the same time, the pus is mixed with more or less abundant catarrhal sputum, provided the abscess has perforated slowly. If perforation take place suddenly, large quantities of pure pus are expectorated, which contains microscopic elastic fibers and hematoidin, cholesterin, and fatty crystals, besides lung pigment and bacteria (Fig. 278).

SPUTUM IN PERFORATING EMPYEMA

This usually resembles the sputum of a pulmonary abscess very closely. Elastic fibers, if present, occur in very small numbers. Hematoidin and other crystals may be present. (See Fig. 278.) The sputum of an odorless empyema may have a very foul odor after perforation, because the empyema cavity becomes infected with saprophytic bacteria from the lung.

SPUTUM IN PUTRID BRONCHITIS

This is more or less purulent, with a foul odor and abundant bacteria, but without any elastic fibers.

SPUTUM IN BRONCHIECTASIS

The sputum of sacculated bronchiectasis is mucopurulent, but it is often more profuse than is a simple catarrhal sputum, and it is expectorated periodically. Expectoration is easier in certain positions of the body, according to the location of the bronchiectasis. The odor is frequently foul. Its microscopic peculiarities

are quite like those of the sputum of putrid bronchitis. In diffuse bronchiectasis the sputum resembles sometimes the above type, at other times that of simple catarrhal sputum. The odor may or may not be foul.

SEROUS SPUTUM IN PULMONARY EDEMA AND IN PERFORATING SEROUS PLEURISY

The sputum in edema of the lung is colorless or faintly tinged with blood, foamy, and somewhat opaque, and usually profuse. It separates, upon standing, into a lower liquid and an upper foamy layer. The latter is quite abundant. At the bottom there may settle a very thin layer of morphologic constituents, which consist partly of leukocytes and lymphocytes transuded with the edematous fluid, and partly of other elements from some other affection of the lung, present at the same time (bronchitis, pneumonia). Otherwise the sputum of pulmonary edema consists chiefly of pure or slightly bloody serum, which contains a moderate amount of albumin (demonstrated by boiling and addition of acid). The sputum raised after a paracentesis for pleurisy may present all the characteristics of that from a case of pulmonary edema. The French call this expectoration "albumineuse." It is nothing more than the product of an acute edema of the lung following the sudden removal of pressure from the pulmonary vessels. Fortunately, however, paracentesis is not generally followed by any severe symptoms. If a serous pleural exudation perforate the lung and is then expectorated, the sputum will resemble that in edema.[1] This is, of course, very rare, but it does occur. The sputum from a pleurisy can in such cases be differentiated by means of its greater albumin content from the sputum in edema, the fluid, as a rule, becoming solid after addition of acid and boiling.

SPUTUM IN VARIOUS KINDS OF PULMONARY HEMORRHAGE AND IN HEMORRHAGIC INFARCTION OF THE LUNG

In marked hemorrhages of the lung proper, such as occur after injury, or in tuberculosis or new-growths, the sputum may consist chiefly of blood. It is usually bright red, whether it comes from the pulmonary artery or from one of the veins or capillaries, because the dark venous blood of the pulmonary artery in its course along the bronchi has usually been sufficiently aërated to be rendered more or less arterial. The intimate admixture of the blood with air in the lung causes the frothy nature of the expectoration. This frothy appearance and bright red color, and the fact that the blood is coughed up, are usually characteristic enough to establish the diagnosis that the seat of the hemorrhage is in the lung.

It is, however, sometimes difficult to determine whether the blood comes from the lung or from the digestive tract, especially from the stomach. Differentiation is usually easy, provided the physician himself sees the hemorrhage occur, but it is often very hard to judge from the patient's statements. In the first place, the patient takes no special note of his condition, on account of excitement, and is not sure whether he coughed or vomited the blood; and, in the second place, vomiting may be produced by the violent paroxysms of coughing accompanying a pulmonary hemorrhage; or, on the other hand, vomiting blood from the stomach may start a fit of coughing, on account of the aspiration of blood into the larynx.

When in doubt, reliance must be placed upon the objective examination of the blood. Frothy, bright-red blood favors the diagnosis of a hemorrhage from the lung. Blood from the stomach is more apt to be dark (methemoglobin and hematin), partly coagulated, and not foamy, because it has been more or less digested. Bright-red blood may come from a hemorrhage from the stomach where an ulcer has eroded an artery of the stomach and the blood is vomited in such large quantities that it is still bright red without having undergone any change. On the other hand, in exceptional cases dark blood, without admixture of air, is observed in a hemorrhage from the lung when the eroded vessel is a large branch of the pulmonary artery, from which the dark venous blood has been expectorated so quickly that it has undergone no change.

The reaction is frequently mentioned as a differential point between blood from the lungs and that from the stomach. The former is said to be alkaline; the latter acid, on account of the admixture of gastric juice. But this is true only

[1] Sahli, Ueber, die Perforation seröser Exsudate, etc., Mittheilungen aus klin. u. med. Instituten der Schweiz, 1894, vol. i, part 9.

when the stomach contains a considerable quantity of acid secretion at the time that the blood is vomited.

No one point can be considered absolute in differentiating between a hemorrhage from the lung and one from the stomach. Nevertheless, it is usually not very difficult to decide in any given case. Examination of the patient is more important than is the consistence of the blood, and especially a careful attention to the symptoms preceding or following the hemorrhage. A patient with hemorrhage from the stomach usually gives a history of previous gastric difficulty, or such a disturbance can be determined after the hemorrhage has taken place. Patients who have had a hemorrhage from the stomach usually pass blood in their movements. On the other hand, a patient with hemorrhage from the lung has usually been subject to a cough before or after the bleeding. The expectoration is almost always blood-tinged for days after the hemorrhage, either blood red or brownish. If all these points be taken into consideration, the diagnosis will not, as a rule, be difficult.

Slight hemorrhages from the lung, as contrasted with a true *hemoptysis*, will cause more or less tinging of a catarrhal sputum. The blood is not so intimately mixed with the expectoration as it is in the sputum of pneumonia, but occurs in streaks. A sputum of this sort does not always come from the lung, and so often causes patients quite unnecessary worry. It is very uncommon to have hemoptysis proper from the larynx or trachea (for the simple reason that there are no large vessels there). But slight, streak-like hemorrhages may arise from the small vessels in the mucous membrane of the larger bronchi, the trachea, the larynx, or of the pharynx itself. Bronchitis may sometimes give rise to a hemorrhagic sputum, for, during the last influenza epidemic, some patients expectorated for weeks a blood-tinged catarrhal sputum without any especial disturbance of the general condition. It is not always possible to distinguish between these various conditions. Besides this, it must be mentioned that the clots coming from an epistaxis which has occurred during sleep may become mixed with the sputum in the pharynx as the blood is swallowed. Such sputum may be erroneously attributed to a pulmonary hemorrhage. A careful examination of the anterior and posterior nasal passages will generally settle the diagnosis.

Most cases of hemorrhagic infarction of the lung present a typical sputum, dark and bloody, and resembling pure blood. In its tenacious consistence, however, it resembles the sputum of pneumonia. In fact, the sputum in these cases is an intimate mixture of blood with a tenacious exudation. Besides this typical form, the sputum of infarction shows many varieties, in some cases resembling the sputum of tuberculous hemoptysis, in other cases that of pneumonia.

EXAMINATION OF THE BLOOD

The examination of the blood furnishes a number of important diagnostic data. Several of the methods are so simple that they can be employed at the bedside in daily practice, whereas others are too complicated for such a purpose.

METHOD OF OBTAINING BLOOD FOR EXAMINATION

A few drops are sufficient for microscopic examination, for the determination of the coagulability, for the estimation of the alkalinity of the blood, for counting the cells, for serum reactions, etc. This may be obtained by puncturing the tip of a patient's finger with a needle, or, better, sharp lancet.[1]

Francke's instrument[2] (Fig. 294) pierces the skin very rapidly with

[1] The blood is often taken from the lobe of the ear, but this is of no particular advantage.

[2] See Deut. med. Woch., 1889, No. 2, p. 27. [A similar one is made by Baker & Co., of London. It is smaller and very satisfactory. (See Fig. 295.)—Ed.]

a narrow, needle-like lancet to a depth which can be readily regulated. It does not cause serious pain. Pressing on the lever suddenly releases a spiral spring in the interior of the instrument, which drives the point of the lancet into the skin to a depth regulated by the guard (*d*). The blade may be easily removed and cleansed. The instrument may be adjusted so as to obtain sufficient blood where a larger quantity is needed (alkalinity). The author formerly strongly recommended this instrument in practice (though at first sight it may seem unnecessary), because it reduces the inconvenience and annoyance of obtaining the blood to a minimum. Unfortunately, it has recently been so badly made that after a short time it refuses service. Very often it is impossible to unscrew the blade, so that it cannot be thoroughly disinfected. The author has, therefore, constructed a simpler, cheaper, and more compact instrument,[1] in which the puncture is also made by a lancet. It is, however, made by manual instead of spring pressure; its depth is regulated by an adjustable guard. Since the depth of the puncture cannot exceed the length of the lancet exposed, the stab may be very quickly made, and is no more disagreeable to the patient than when Francke's needle is employed. Since the blade can be easily taken out, the instrument may be readily disinfected. Dr. J. Ries has also devised a lancet whose blade is a sewing or two-edged needle (easily replaced) which may be sterilized in the flame and thrown away after use. A number of extra needles are furnished with the instrument at low cost.[2]

Fig. 294.—Francke's needle for removing blood for clinical purposes (about one-half its actual size).

Before taking the blood it is important to dry the skin carefully, for otherwise the drop spreads out and filling the pipet becomes difficult. Sterilization of the skin is unnecessary.

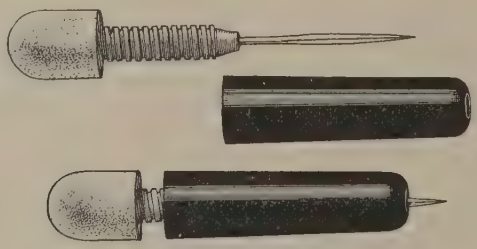


Fig. 295.—Blood-needle.

If several cubic centimeters of blood be required, wet-cupping may be employed; but since the blood coagulates so rapidly that certain methods of investigation are difficult of execution, it is better to use a cannula inserted into a vein. An ordinary hypodermic syringe with a

[1] Made by Buchi, in Bern.
[2] This instrument with extra needles may be obtained from M. Schärer & Co., in Bern, for 4 francs.

large needle may be all that is required; but when quite large amounts are necessary, they are best obtained by a larger cannula, through which the blood flows directly from the vein. A piece of tubing is attached to the end of the cannula. The cannula should have a lumen of at least 1 mm. Its length should not exceed 4 cm., otherwise the flow of blood will soon be interrupted by coagulation; moreover, a longer cannula is difficult of manipulation.[1] Whether a needle or a larger cannula is used, it should be very sharp, as the vein may easily be pushed aside by the point. In introducing the cannula the median vein is selected, a fillet is placed about the arm, and the instrument is thrust toward the heart, since this is usually more convenient, and as nearly parallel as possible to the cutaneous surface. The author has convinced himself that this method is not adapted to the quantitative examination of the blood, since the stasis produced by the fillet quickly changes the composition of the blood withdrawn, particularly in respect to the proportion between the solid constituents and the water. This condition of affairs may be avoided, however, by loosening the fillet for one to two minutes before the blood is withdrawn. One does not, however, always succeed in getting large amounts of blood by this method.

QUANTITY OF THE BLOOD; DIAGNOSIS OF HYDREMIC PLETHORA; ESTIMATION OF THE ABSOLUTE AMOUNT OF BLOOD IN MAN

The blood in man is estimated to be about one-thirteenth of the body-weight, but it is very probable that this ratio may be changed under pathologic conditions. There are as yet no positive data, although it would be of the greatest clinical interest to have accurate information upon this point. After acute losses of blood the quantity doubtless remains diminished, perhaps, however, only for a short time. Furthermore, when the body is deprived of water, the liquid portion of the blood is utilized, the blood becomes somewhat thicker, and is diminished in quantity. This probably occurs in cholera and in the acute infantile diarrheas, judging from the great amount of water lost, the slight distention of the vessels, and the increased hemoglobin. Quantitative spectroscopic examinations and hemoglobin estimations have recently shown that the concentration of the blood increases after marked perspiration and after the use of saline cathartics and diuretics, due to the loss of water.

The demonstration of hydremic plethora (*i. e.*, an increased quantity of blood, due to the retention of water) is of particular clinical interest. This demonstration is sometimes possible from a determination of the hemoglobin percentage (see p. 742 et seq.), which falls when the water is retained. It is clear, however, that it is possible to base a diagnosis of hydremic plethora upon the oligochromemic character of the blood only when the latter develops acutely under the observation of the physician, and when hemorrhage or other common causes of anemia can be excluded. With these limitations, the fall of the hemoglobin percentage is a useful indication of hydremic plethora, since hemoglobin cannot quickly enter or leave the vessels, as can the soluble constituents of the blood. It consequently follows that hydremic plethora or retention of water in the blood is frequently to be recognized only by the lowering of the hemoglobin percentage, while the specific gravity, the dry residue, and the osmotic pressure remain normal, since the dissolved constituents, particularly the salts, may remain in the blood. In cases of nephritis, for example, the hydremo-plethoric blood very commonly exhibits even an increased osmotic pressure.

The conditions of so-called "bloodlessness"—the various types of *anemia*—are by no means necessarily due to a deficient quantity of blood, as has been previously supposed, and as is indicated by the name. But the constant sign of anemia

[1] Such cannulæ, which are also used in the Bern Clinic for blood-letting with great advantage, may be obtained from the instrument made by Klöpfe in Bern. They are made in platinum and iridium, as well as in nickeled steel. The former may be sterilized in the flame.

(oligochromemia, pallor of the blood) is due to a diminution in the percentage of blood-pigment. Traumatic anemia, due to loss of blood, is, of course, at the first associated with a diminution in the quantity; but even this condition is rapidly changed to a simple oligochromemia, the blood lost being rapidly replaced by absorption of lymph from the tissues. In pernicious anemia the quantity of blood seems usually to be diminished; in chlorosis, often increased (p. 734).

ESTIMATION OF THE BLOOD-MASS ACCORDING TO KRONECKER AND KOTTMANN

Although, from variations of the hemoglobin content of the blood, it is possible to form some idea of an increase or decrease of the blood-mass, we still lack a clinical method for its exact determination. This is not surprising when we consider that even in animals such estimations are attended with extreme difficulty.

Kottmann[1] has recently described a method that can be applied clinically. This procedure consists of intravenous injections of a known amount of isotonic salt solution. From differences in the content of red blood-corpuscles, before and after the infusion, conclusions as to the amount of blood may be drawn, as, the greater the resulting dilution, the smaller the quantity of blood, and vice versâ. Kronecker and Sander in 1881 used a similar method on the dog, but it was soon discarded These authors counted the blood-corpuscles in a known amount of blood, while Kottmann estimates the corpuscular volume before and after infusion by means of a hematocrit. (See p. 767 et seq.) This instrument was especially constructed for accurate work, and requires a very rapid electric centrifuge with large radius. The infusion is given by means of a needle thrust through the skin directly into one of the veins of the arm. In order to get accurate results, Kottmann advises the use of a salt solution made isotonic with the blood of the person to be examined, according to the method of Hamburger or Dreser. (See Kottmann's original article, *loc. cit.*) For approximate determinations in the sick, in whom the osmotic tension of the blood is assumed to be normal, a 0.9 per cent. sodium chlorid solution is considered isotonic, and is used for the infusion. For the estimation of the corpuscular volume, blood is obtained by a prick from the finger or lobe of the ear. To prevent coagulation, Kottmann adds some hirudin to the blood before centrifuging, and also rubs a few crystals over the wound, so that the blood comes in contact with it at once. Between the infusion and the second estimation five minutes must be allowed to secure a thorough mixing of saline and blood. Three hundred cubic centimeters of sterile salt solution at body temperature are slowly infused, five minutes being consumed by this procedure. By this method Kottmann found that the blood-mass in normal individuals varied from one-twelfth to one-thirteenth of the body-weight. This agrees with the usual assumption. To be sure, this method, as all similar ones, gives only the circulating blood-mass, *i. e.*, the amount of blood which by its active circulation mixes intimately with the salt solution. Naturally, in those vascular areas where the circulation is slow or more or less stagnated, the mixture is incomplete, and the results are, therefore, inaccurate. A drawback to this method and one that may hinder its clinical application is that patients usually experience a rise of temperature after the infusion, although without other abnormal symptoms. This shows that the procedure cannot be considered entirely indifferent. The author advised Dr. Kottmann to experiment, in order to determine whether, by means of a smaller amount of fluid or the use of another salt solution, such as Ringer's fluid or some other similar and more complicated mixture, this method could not be made so indifferent as to commend itself in clinical practice. These experiments have, unfortunately, not yet been attempted. In addition, the ordinary clinical centrifuge must be improved, according to the suggestion of Kottmann, although the employment of the hematocrit could easily be replaced by the method of Kronecker and Sander, namely, counting large numbers of corpuscles. This latter procedure for such purposes is generally considered more accurate.

ESTIMATION OF THE BLOOD-MASS BY HALDANE AND J. LORRAINE SMITH

Haldane and Smith,[2] following the method of Gréhant and Quinquaud, have determined the human blood-mass by the inhalation of definite non-toxic amounts of carbon monoxid. The principle of the method is as follows: The oxygen capacity

[1] Kottmann, Arch. f. exp. Path. u. Therap., 1906, vol. liv.
[2] Jour. Physiol., vol. xxv, p. 331.

of the blood of the individual under examination is first determined, this being identical with the capacity of this blood for carbon monoxid. Since the oxygen capacity is proportional to the pigment content, the former is determined by a colorimetric method, in which the blood of the person under experiment is compared, by means of a colorimeter, with ox-blood, the oxygen capacity of which has previously been found by the ferricyanid method.[1] The person to be examined inhales, through a mouth-piece, a measured and harmless quantity of CO (100 to 150 cc.) from a rubber bag, which is supplied with O_2 from a cylinder. The patient also exhales into this bag through a vessel containing soda-lime. CO from a graduated vessel is added to the oxygen in measured quantities of about 30 cc. These amounts of CO are forced into the respiration-bag by allowing water to replace the gas in the graduate. When the required quantity of CO has passed into the bag, the stop-cock of the container is turned off, and the patient breathes from the bag, replenished with oxygen from time to time, until all the CO, as shown by chemical tests, has been exhausted. (See the original for this method.) It is then certain that the measured quantity of CO has been entirely absorbed through the lungs by the blood. The expired carbonic acid is absorbed by the soda-lime. A test is now made of the blood of the patient under experiment, and the CO content is determined by the following method (Haldane described this some time ago). A 1 per cent. solution of the blood from which the previous colorimetric determinations were made is used; 2 cc. of this are put into a calibrated test-tube (*a*). In a second test-tube (*b*), of the same caliber, are placed exactly 2 cc. of a 1 per cent. solution of the blood drawn after the CO inhalation. This second tube shows a more intense coloration, on account of the CO present. In a third tube (*c*) are placed 2 cc. of the first blood after saturating it fully with CO. There are now three tubes, with equal quantities of a 1 per cent. solution of the patient's blood, of which the first contains no CO, the second contains the amount of CO derived from the inhalation, while the third is fully saturated with CO. Add, now, from a buret to tube (*a*) a solution of carmin of known concentration, the preparation of which will be given below, until its shade corresponds to that of tube (*b*), and note the amount added—suppose, for example, 0.45 cc. Then continue adding carmin solution to tube (*a*) until its shade corresponds to that of the fully saturated solution of blood in tube (*c*), and again note the total quantity added, for instance, 2.5 cc. The following calculations can then be made: Tube (*a*) contains, after the first addition of 0.45 cc. carmin solution, a total of 2.45 cc., and after the second addition of carmin a total amount of 4.5 cc. The relative quantity of carmin solution first added, as compared with the total quantity added, is in the same proportion to that of the total amount as $\frac{0.45}{2.45} : \frac{2.5}{4.5}$. In order to express this in percentage we make this ratio $= x : 100$. Then $x = 100 \cdot \frac{0.45}{2.45} \cdot \frac{4.5}{2.5} = 33$ per cent. Here x represents the amount of carmin which it was necessary to add, in order to make the shade of the original blood correspond with that of the blood to which CO has been added by inhalation, expressed in percentage of the total amount of carmin, which was needed to make the shade correspond with that of the fully saturated CO blood. Since Haldane has found that these carmin additions are proportional to the corresponding CO content, x expresses the CO content of the blood after the CO inhalation in percentage of the volume necessary for full saturation. After finding these data we calculate the quantity of blood as follows: If, after inhalation of, say, 150 cc., a CO content of 25 per cent. (by volume) of the total amount needed for saturation be found, and if then the amount of CO (or, what comes to the same thing, the amount of O_2) needed for saturation be found with a colorimeter by comparison with ox-blood, of a known O_2 or (CO) capacity, to be 20 in 100 volumes, then the CO content of the blood after CO inhalation equals $\frac{25}{100} \times \frac{20}{100} = \frac{500}{10000} = \frac{1}{20}$ by volume. Consequently, we have to multiply the quantity of CO inhaled by 20 in order to obtain the blood-mass, which in this case would be $150 \times 20 = 3000$ cc. These writers believe that the quantity of CO taken up by the muscles and tissues can be disregarded. The carmin solution is prepared in the following way: One gm. of carmin is rubbed in a mortar with several drops of ammonia, and then dissolved in 100 cc. of glycerin. This stock solution is stable. A 1 per cent. watery solution (which is unstable) must be freshly prepared from this each time before using. This dilution is such that 6 cc. of it, added to 5 cc. of a 1 per cent. ox-blood solution, will give the same shade as the blood solution fully saturated with CO. The writers have found, by means of their method, that, contrary to the usual supposition, the amount of blood in man is but $\frac{1}{26}$ of the body-weight. This disagreement with the

[1] See Barcroft & Morawitz, Deut. Arch. f. klin. Med., 1908, vol. xciii, part 3, where the older literature is mentioned.

higher values obtained by Kottmann, using the salt-solution infusion (1: 12 to 1: 13, see p. 732), is so conspicuous that the CO method must be considered as questionable, on account of the loss of CO in the tissues. The author believes that this method is not altogether clinically safe, for, although the amount of CO employed (Plesch states that at least 100 cc. are necessary) probably would not give rise to disturbances of health in a normal individual, yet such might easily be the case with weak, anemic, or dyspneic individuals.

THE CLINICAL RESULTS OF THE ESTIMATION OF THE BLOOD-MASS

The Haldane-Smith method has been used clinically by Plesch,[1] through the application of a new chromophotometer. He has also found the blood-mass to be normally $\frac{1}{20}$ of the body-weight. In cases of chlorosis he found an increase in the blood-mass. Oerum[2] has also corroborated clinically the experimental evidence of Haldane and Smith. He gives a cut of the apparatus used in this work. He, too found an increase in the blood-mass in chlorosis. In a case of pernicious anemia, however, he found the blood-mass was normal, while in this disease Kottmann found it decreased (*loc. cit.*). It should be noticed that, in the estimation of the blood-mass, one must consider the weight of the body, since, according to Bollinger, the blood-mass normally is in direct proportion to the muscular development and inversely proportional to the development of fat. The estimations, therefore, are necessarily dependent on the condition of the patient.

THE SPECIFIC GRAVITY OF THE BLOOD

Since large quantities of the blood are now easily obtained, the specific gravity of the blood can be determined with greater accuracy by weighing a given volume, making use of the so-called pyknometer,[3] either one already calibrated or a vessel to be calibrated by weighing after it is filled with distilled water. It is obvious that corrections for temperature must be made, in the former case, by bringing the pyknometer, which is filled with blood, to the temperature for which it is calibrated, while in the latter case the vessel, when filled with water, and later when filled with blood, is weighed at the same temperature, generally 15° C. For clinical purposes, however, the specific gravity of the blood can be estimated according to two different methods, using very small quantities of blood. One of these is known as the areometric, the other as the capillary pyknometric, method.

In the *areometric method* (Roy v. Jaksch, Devoto, *et al.*[4]) a drop of blood is placed in fluids of different but known specific gravity, *e. g.*, in different mixtures of water and glycerin. The specific gravity of the blood is the same as that of the mixture in which the drop remains suspended. The influence of coagulation and diffusion militates against this method, and, besides, it is difficult to obtain a great many drops of blood successively from one and the same patient; it has, however, the advantage that it may be performed at the bedside, without any analytic balance.

Hammerschlag's Method. Hammerschlag[5] modified this method by placing a mixture of benzol chloroform, of an average specific gravity of 1050 to 1060, in a test-tube or in a urinometer. A drop of blood is then allowed to fall gently into this mixture, and, according to whether the drop floats or sinks, benzol or chloroform is added until the drop is exactly suspended. The drop of blood can then be easily removed by filtering through a piece of linen, and the specific gravity of the mixture determined with the areometer. The fluid may be saved for further use.

Eykmann[6] has further modified the Hammerschlag method, and thereby has made it more accurate. He has observed that a drop of fluid, although of a different specific gravity, may become suspended in the given chloroform-benzol mixture,

[1] Verhandl. des Cong. f. inn. Med., 1907, p. 584.

[2] Arch. f. klin. Med., 1908, vol. xciii, p. 366.

[3] Ostwald's modification of Sprengel's pyknometer is commonly used. In regard to the employment of this instrument see Ostwald-Luther, Physico-Chemische Messungen, Leipzig, 1902.

[4] Roy, Proc. Physiol. Soc., 1884; Devoto, Zeit. f. Heilk., 1889, No. 11, p. 175; v. Jaksch, Klin. Diagnostik, 1892.

[5] Zeit. f. klin. Med., 1892, vol. xx, p. 444.

[6] Virchow's Arch., 1896, vol. cxliii, p. 457.

but that the height at which the drop comes to rest is different and constant for each different specific weight of the drop. Eykmann, therefore, employs salt solutions, which show very slight differences in specific gravity (for instance, 0.0002), which can be determined by a fine areometer. The solutions are best prepared by mixing two salt solutions of different concentration. In order to avoid mistaking one solution for another, they are colored with traces of different anilin dyes. A drop of each of these solutions will be suspended at a constant height in the chloroform-benzol mixture. A drop of the blood to be examined is also placed in the chloroform-benzol and then compared with the salt solution. The specific gravity of the drop of salt solution, which is at the same height as the drop of blood, shows accurately the specific gravity of the blood. (For details, see the original work.)

In the *capillary pyknometric method* Schmalz[1] employs a capillary tube (capillary pyknometer), 1½ mm. in internal diameter and 12 cm. long, slightly constricted at the ends so as easily to retain its contents. This tube is dried, filled with distilled water, and then weighed. It is then carefully dried with alcohol and ether, filled with the blood to be examined, and weighed again. If c equal the weight of the empty capillary tube, c' the weight of the capillary tube plus the water, and c'' the weight of the capillary tube plus the blood, then $c'-c$ will be equal to the weight of the water, and $c''-c$ will be the weight of an equal volume of blood. Therefore the specific weight of the blood will be $\frac{c''-c}{c'-c}$.

Experiments at the Bern Clinic have proved that this method is easy and accurate if scales weighing to $\frac{1}{20}$ mg. be used.

The results of determining the specific gravity of the blood thus far have shown that it is diminished in all anemic conditions (oligochromemia), and in some other cachectic conditions (nephritis, digestive disturbances), although the percentage of hemoglobin need not be diminished. The normal figures vary between 1.0455 and 1.0665. In men it averages about 1.0550; in women, 1.0535; and in children, 1.0512 (Peiper).

Hammerschlag[2] advocates a method of estimating the specific gravity of the *blood-plasma*, based upon the above-described areometric principle. The blood is drawn into a capillary tube 3 to 4 cm. long and 1 to 2 mm. in diameter. The tube should be previously washed out with a 3 per cent. solution of sodium oxalate, to prevent coagulation, and then blown out. Both ends of the tube are closed with wax, the tube is set in a vertical position, and the blood is allowed to settle. After the blood-corpuscles have separated from the plasma, the capillary tube is filed in two at the point where the two layers meet, and the plasma is examined according to Hammerschlag's areometric method. The admixture of the sodium oxalate solution causes a slight error in the result, but so slight, according to Hammerschlag, that it need not be considered (?). The specific gravity of blood-serum may be determined in a similar way. The blood is allowed to coagulate in the capillary tube without adding the oxalate, and to stand until the clot has pressed out a sufficient quantity of serum. According to Hammerschlag, the specific gravity of blood-serum varies but very little from that of the plasma. The specific gravity of plasma in a healthy individual ranges from 1029 to 1032. It is diminished in conditions associated with hydrops, especially in nephritis. In these conditions, however, the specific gravity of the plasma may be increased, since in addition to water, proportionately larger quantities of the solid constituents may be retained in the blood.

Eykmann's method, described above, can, of course, also be used in determining the specific gravity of the plasma or serum. In order to obtain plasma it is best to employ a small quantity of hirudin (about 1 mg. to 5 cc. of blood), which serves to prevent the coagulation of the blood without essentially affecting its specific gravity. The gas-content of the blood influences the specific gravity of its fluid portion, depending upon the exchange of ions between the corpuscular and plasma portions of the blood; hence, we must observe the same precautions in these estimations as in the estimation of the reaction of the blood-plasma and blood-serum (see below): that is, the blood must be centrifuged for obtaining serum or plasma with the most careful avoidance of the admission of any air, or it must be shaken with air just as carefully, and in giving results one must state which of these methods was used.

[1] Deut. Arch. f. klin. Med., 1890, vol. xlvii, p. 145, and Deut. med. Woch., 1891, No. 17, p. 555.

[2] Zeit. f. klin. Med., 1892, vol. xxi, p. 475.

REACTION OF THE BLOOD

The normal reaction of the blood is alkaline, the degree of alkalinity varying under pathologic conditions. The alkalinity of arterial is somewhat greater than that of venous blood. According to Zuntz, it is decreased after coagulation. A decrease in alkalinity is found in severe (pernicious) anemia, but not in chlorosis (Emerson; see, however, p. 738), in fevers, and in acidosis arising from diabetes mellitus or cachexia. According to Cantani, blood may become acid in cholera.

The peculiar color of blood renders titration with indicators very difficult, so that an attempt has recently been made to estimate the degree of alkalinity by determining the amount of carbonic acid contained in the blood, on the ground that this amount depends essentially upon the alkalinity. Theoretically, this deduction is questionable, and, moreover, the method of estimating carbonic acid is too complicated for clinical purposes and requires altogether too much blood.

The blood owes its alkalinity essentially to the presence of sodium carbonate, alkaline sodium phosphate, and the alkaline earths. Löwy and Zuntz[1] divide this alkalinity into two parts, one of which depends upon the diffusible alkaline salts and the other the acid-binding value of protein. Brandenberg[2] estimates the first portion by bringing the blood into contact with alkalinized physiologic salt solutions of varying degrees of alkalinity by means of a diffusible membrane, until the alkalinity of the blood does not change by diffusion. He found that for blood, as a whole, the diffusible alkali is to the total alkali as 1 is to 5; for the serum as 1 is to 2; for the corpuscles, as 1 is to 8. According to Brandenberg, the diffusible alkali of the blood as a whole (alkali tension of the blood measured by means of the alkalinity of a soda solution in contact with which the blood neither gives off nor takes up alkali), is equal to 60 mg. NaOH for every 100 cc. of blood. (Compare this with the normal total alkalinity of laked blood given on p. 738.) The alkali tension of the "whole blood" is reduced in diabetes mellitus (acidosis), in uremia, in pneumonia, and in certain forms of nephritis. Brandenberg's method of estimating the diffusible alkalis is too complicated for clinical purposes. Hamburger has, however, proposed a process by which we can determine the total and the diffusible alkali separately. (See p. 739.) In the technic of obtaining blood for alkali titration one must take into account the fact, proved by Hamburger, that the gas-content of the blood (CO_2 and O_2) markedly influences the division of the ions between the blood-corpuscles and the plasma. If one wish to determine the reaction of the plasma or serum without altering the relations artificially, he must obtain the blood without the admission of any air, and collect plasma and serum respectively in sealed tubes. For this reason Hamburger defibrinates the blood by shaking it, in a flask completely filled by blood, with glass beads. Since large quantities of blood can be obtained from man only by means of a temporary obstruction of a vein, whereby the CO_2 content is artificially changed, the precautionary measures mentioned above are useless for methods which require large amounts of blood and, on the contrary, it is advisable to shake the blood with air, so that it becomes as saturated with O_2 as possible, in order that comparable results may be obtained. For the methods in which small quantities of blood are used the influence of air cannot be eliminated, and here also it seems advisable to give the air the freest access possible. It, therefore, appears that there is no satisfactory method of studying the division of alkali between the corpuscles and plasma as they are found within the body.

The teachings of physical chemistry in medicine have brought forth certain complications with regard to the conception of alkalinity, since very frequently the idea of alkaline reaction is confused with the idea of the hydroxyl ion content. In the latter case, the blood can practically be considered as neutral, for, according to recent experiments, there exists no noticeable excess of the OH- over H-ions. But there is not on this account any reason for giving up the old idea of the alkaline reaction in favor of the hydroxyl ion theory. Both are equally important properties, but the estimation of the reaction from the action on certain known indicators has the priority, and it would seem to be unwise to replace suddenly an old and satisfactory idea with a new one. This can only lead to misunderstandings. The reader can compare with this the author's similar remarks on the reaction of the urine.

[1] Pflüger's Arch., 1894, lxxxviii.

[2] Zeit. f. klin. Med., 1902, vol. xlv, pp. 157–200, and Deut. med. Woch., 1902.

TITRATION OF OPAQUE BLOOD (after Landois-v. Jaksch)[1]

This method consists in a modified titration of minute quantities of blood. A series of tartaric acid solutions of known acidity is kept in stock. A measured small quantity of blood—for instance, 0.1 cc.—is added consecutively to 1 cc. of each of these acid solutions. They are stirred quickly, and the reaction is tested with some very sensitive litmus paper. Titration with litmus has, of course, the disadvantage that this dye does not react acid to CO_2. The degree of acidity of the tartaric acid solution which is exactly neutralized by the blood indicates the alkalinity of the blood.

Von Jaksch employs the following 18 test solutions to carry out this method:

Solution	1	contains in	1 cc.	0.9 cc.	$\frac{1}{100}$	Normal tartaric acid and	0.1	concent.	sol. of	Glauber's	salt.
"	2	"	" 1 "	0.8 "	"		0.2	"	"	"	
"	3	"	" 1 "	0.7 "	"		0.3	"	"	"	
	etc.			etc.			etc.				
"	9	"	" 1 "	0.1 "	"		0.9	"	"	"	
"	10	"	" 1 "	0.9 "	$\frac{1}{1000}$		0.1	"	"	"	
"	11	"	" 1 "	0.8 "	"		0.2	"	"	"	
	etc.			etc.			etc.				
"	18	"	" 1 "	0.1 "	"		0.9	"	"	"	

The Glauber's salt solution is added instead of distilled water to preserve the red blood-corpuscles and make the solution permanent.

$\frac{N}{100}$ and $\frac{N}{1000}$ tartaric acid solutions are obtained by diluting a $\frac{N}{10}$ solution which contains 7.5 gm. tartaric acid in 1 liter water.

Von Jaksch obtains the specimen of blood by a wet-cup. Miss Freudberg[2] undertook to determine the alkalinity of the blood in cases at the Bern Clinic. She employed Francke's needle (p. 729), but used only 0.05 cc. of blood, because it was difficult to get 0.1 cc. from so small a puncture. The blood is sucked into a capillary pipet. Immediately after removal it is blown into a watch-glass containing 0.5 cc. of tartaric acid solution of an average degree of acidity. The mixture in the watch-glass is stirred rapidly with a little glass rod, and the reaction tested with litmus-paper. If acid, the experiment is repeated with a weaker solution until the point is reached when the amount of blood employed neutralizes the acid solution exactly. It is best not to proceed from one solution to the next, but to skip several, so that the outside limits between which the degree of acidity lies may be quickly obtained. Care must be taken to remove the blood as rapidly as possible, as a considerable amount of alkalinity is lost by chemical changes outside of the vascular system. Especial care must also be devoted to preparing a very sensitive litmus paper. (See text-books on Chemistry.[3]) The method of using litmus paper is as follows: A drop of the mixture of blood and acid is dropped upon the paper with a glass rod, and the fluid immediately removed with a piece of white filter-paper which is known to be neutral. The blood-pigment, which is the disturbing factor, is taken up by the filter-paper, leaving an unmistakable spot on the litmus paper provided neutralization is not complete. Only neutral litmus paper can be used for testing, because the blood-pigment, even after it has been taken up with filter-paper, renders it impossible or very difficult to recognize the reaction upon red acid litmus paper. For this reason neutral (violet) litmus paper should be used. Successively weaker solutions of tartaric acid should be tried until no red spot remains.

It has not yet been definitely determined whether this method of blood-titration with litmus paper gives reliable results. The uncertainty depends upon the well-known peculiarity of litmus pigment to react amphoterically to mixtures of both alkaline phosphates contained in the blood (primary and secondary).

We have already referred to this difficulty under Acidimetric Titration of the Urine. Besides, despite the addition of salt solution to preserve the cells, they gradually become acid in reaction. This happens, to an increased degree, the longer it takes to determine the reaction, and, as a consequence, the results are inexact.

[1] Landois, Eulenburg's Realencyklopädie, 1895, vol. iii, p. 161, second ed.; v. Jaksch, Zeit. f. klin. Med., 1887, vol. xiii, p. 350.

[2] Freudberg, Einfluz von Sauren und Alkalien auf die Harnacidität, Virch. Arch., 1891.

[3] Fresenius, Qualitative Analyse, 1895, sixteenth ed., p. 100, note.

The principal fact obtained by von Jaksch with this method, and corroborated by Miss Freudberg, is that the alkalinity of the blood diminishes in all anemias. (In regard to chlorosis, however, see p. 736.) Von Jaksch found the same to be true for diabetes mellitus, for uremia, and for fever.

The normal alkalinity of the blood determined in this way corresponds, according to von Jaksch, to 0.26 to 0.30 sodium hydroxid, for 100 cc. of blood.

TITRATION OF LAKED BLOOD (after Löwy[1] and Engle)

In order to obviate the difficulty that red cells gradually, and, therefore, to an unknown degree, enter into the reaction through contact of the blood with the tartaric acid, Löwy has proposed to lake the blood before titrating, thereby at once completely admitting the red cells to the reaction. Besides this, he employs lacmoid instead of litmus as an indicator. A flask provided with a long, narrow, partially graduated neck, capable of containing 50 cc., is filled with 45 cc. of 0.25 per cent. solution of oxalate of ammonia and 5 cc. of blood. This solution of oxalate of ammonia lakes the blood, and at the same time prevents coagulation. Titration is performed with a $\frac{N}{25}$ tartaric acid solution (see p. 737) and lacmoid[2] paper, which has been saturated with a concentrated solution of magnesium sulphate. The 5 cc. of blood may be taken from a vein. (See p. 731.) If so, however, errors due to stasis occur. With fresh human blood Löwy's values varied between 400 and 600 mg. NaOH per 100 cc. of blood. These are higher values than von Jaksch obtained with unlaked blood. H. Strauss'[3] values were medium, 300 to 350 mg. per 100 cc. of blood.

S. Engel[4] modified this method by using a mélangeur (see p. 854), diluting 0.05 of blood 100 times with neutral distilled water. With this mixture in a small beaker he then titrates from a buret, graded into $\frac{1}{20}$ cc., dropping with great care a $\frac{N}{75}$ tartaric acid solution (1 gr. of tartaric acid to 1 liter of water). The end-reaction is tested after the addition of each drop from the buret by wetting a piece of lacmoid[5] paper with one drop of the solution from a glass rod, and then determining the moment when the yellowish drop (hemoglobin) shows a sharp red line around its margin. Engel's and Löwy's results correspond. The relation of lacmoid pigment to mixtures of primary and secondary alkaline phosphates should be more carefully examined before any judgment is formed as to the reliability of Löwy's or Engel's method. The close correspondence of their values with those of Salkowski (see below) is in favor of their accuracy.

From a practical standpoint, it is interesting to note that Magnus-Levy,[6] by the use of Löwy's method in diabetic coma, has observed extraordinary marked diminutions of the alkalinity of the blood—diminutions corresponding to 220 to 260 mg. NaOH to 100 cc. of blood. He attributes this diminished alkalinity partly to neutralized carbonates and partly to the combination of the proteins with acids, which consequently lessens the quantity of acid to be neutralized by titration.

SALKOWSKI'S METHOD OF DETERMINING THE ALKALINITY OF THE BLOOD

Salkowski[7] has recently announced a method of determining the alkalinity of the blood which has the advantage of avoiding direct titration, with all its associated difficulties (color of the blood, uncertainty of the indications in titration in phosphate mixtures). Schlösing's apparatus for determining the amount of ammonia in urine is employed. (See p. 652.) A known quantity of sulphate of ammonia is added to the blood, the alkalinity of which is to be determined, and the amount of ammonia liberated from the alkalis of the blood is then estimated by Schlösing's method. The technic is as follows: Twenty gm. of finely pulverized sulphate of ammonia are placed in the large lower dish of Schlösing's apparatus, and then

[1] Pflüger's Arch., vol. lviii, Centralbl. f. Wissensch., 1894, No. 45.
[2] See Böckmann, Chem.-techn. Untersuchungsmethoden, Berlin, 1893.
[3] Zeit. f. klin. Med., 1896, vol. xxx.
[4] Berlin. klin. Woch., 1898, vol. xiv, p. 308.
[5] Furnished by Dr. Wartenberg, Apothecary, Berlin, SO., Reichenbergerstrasse 63.
[6] Arch. f. exp. Pathol., 1899, vol. xlii, p. 197.
[7] Centralbl. f. d. med. Wissensch., 1898. Ref. in Maly's Jahresbericht, 1898, and Waldvogel, Deut. med. Woch., 1900, No. 43.

dissolved by adding 20 cc. of water. Ten cc. of a $\frac{N}{4}$ solution of sulphuric acid are placed in the upper dish. Ten cc. of blood are then poured into the lower dish with the ammonium sulphate. It is well to add to the blood, at the moment it flows into the graduate in which it is caught, a 1 per cent. solution of sodium oxalate, so as to prevent coagulation. The blood is mixed with the solution of ammonium sulphate, and the globe placed over it as soon as possible.

After five or six days all the ammonia that has been freed has been taken up by the sulphuric acid, and can then be estimated by titration. The entire quantity of sulphuric acid must be used in the titration because, as has been pointed out by Waldvogel, the volume of the acid may change on account of water being given off and combined with the sulphate of ammonia solution.

The technic can be modified by using the Krüger-Reish method for estimating ammonia. (See p. 652.)

Waldvogel gives as normal values for men 350 to 400 mg. NaHO per 100 cc. of blood; for women, 300 to 350. In fever and also in anemia the values were lower. The blood-corpuscles doubtless enter into the reaction in this method. The correspondence of the values found by Waldvogel with those obtained by Löwy would seem to support the value of the method.

Dare's Spectroscopic Method for the Determination of the Alkalinity of the Blood

Dare[1] has recently suggested a method of determining the alkalinity of the blood by titrating laked blood with a $\frac{N}{1000}$ tartaric acid solution. The end-reaction in this method is the disappearance of the characteristic spectrum of hemoglobin and its replacement by that of methemoglobin, the author assuming that the disappearance of the hemoglobin spectrum is coincident with neutralization. Further investigations are necessary, however, to determine the utility of this method, since it has not yet been conclusively shown that the hemoglobin is not destroyed before complete neutralization, and, furthermore, the spectroscopic changes dependent upon variations in the reaction are quite slow in their appearance.

HAMBURGER'S METHOD FOR THE ALKALI TITRATION OF THE BLOOD

With especial reference to the estimation of the diffusible alkalis, Hamburger[2] first titrates the "whole blood" which has been laked, and then the serum after the method of Löwy with a $\frac{N}{25}$ tartaric acid solution (see p. 737), using lacmoid as an indicator. By this means he determines the total alkalinity of the liquid in question. He then estimates the diffusible alkali in another portion of the same liquid by a method to be described later. By subtraction of the diffusible from the total alkali he determines the non-diffusible alkali. With regard to the influence of the access of air, compare p. 736. The method, which Hamburger employs for the titration of the diffusible alkali, is as follows: One hundred cc. of the blood or serum to be examined are mixed with double that quantity of 96 per cent. alcohol. The precipitate, which contains the non-diffusible alkali in the form of albuminates and analogous substances, is filtered out and washed with alcohol. The original filtrate and washings are collected and placed on a water-bath to drive off the alcohol. Water is then added to make 100 cc., and this is then titrated in the usual way with lacmoid and $\frac{N}{25}$ tartaric acid solution. These examinations show that "whole blood" contains much more alkali than the serum, that the non-diffusible alkali is greater in per cent. by weight in both, and that in both the content of diffusible alkali increases by shaking with CO_2.

ESTIMATION OF THE ION-CONCENTRATION OF THE BLOOD BY FRIEDENTHAL AND SCHULTZ

Friedenthal[3] has shown that, aside from the procedures which, on account of their complicated technic, are unsuitable for clinical purposes, the ion-concentration, employing the newer physico-chemical definition of reaction (see p. 736, note 1), can also be more accurately estimated with the aid of indicators. Since the different indicators furnish different dissociation constants, it is possible, according to Frieden-

[1] Proc. Pathol. Soc. of Philadelphia, April, 1903.

[2] Osmotischer Druck u. Ionenlehre, 1902, vol. i, p. 308.

[3] Estimation of the Reaction of a Liquid by Means of Indicators. Zeit. f. Electrochemie, 1904; Fels, ibid., 1904, and Salesski, ibid., 1904.

thal, to find characteristic color changes of certain indicators for the different ion concentrations. For clinical purposes of blood-examination the method of I. H. Schultz [1] is available. This writer prepares, by means of a method which cannot be described here, four acid solutions from hydrochloric acid and sodium acetate, and four basic solutions from barium hydroxid and ammonium chlorid, the ion-concentration of which he computes as follows:

Acid:	$1.0 \cdot 10^{-4}$	$2.0 \cdot 10^{-5}$	$3.0 \cdot 10^{-6}$	$2.5 \cdot 10^{-7}$
Basic:	$0.8 \cdot 10^{-7}$	$2.0 \cdot 10^{-8}$	$9.0 \cdot 10^{-9}$	$7.0 \cdot 10^{-10}$

The given ion-concentrations are calculated for the H-ion of the acid solution, and for the basic solution the OH-ions are calculated as equivalent H-ions. He also prepares saturated solutions of the following named indicators, by dissolving about 2 gm. of each in 200 cc. of distilled water at 30° C. and then filtering. Schultz now tested the action of these solutions, made up corresponding to their ion-content upon these indicators as follows: Of the indicator solution, 0.1 cc. was used in a small white dish of porcelain with 0.02 cc. of the ion solution, and the reaction observed. From this he worked out the following tables:

Acid.

	HCl : H-ions.			
	$1.0 \cdot 10^{-4}$	$2.0 \cdot 10^{-5}$	$3.0 \cdot 10^{-6}$	$2.5 \cdot 10^{-7}$
Anilin violet	Green.	Greenish blue.	Bluish green.	Bluish violet.
Anilin red	Blue.	Blue.	Blue.	Violet brown.
Anilin orange	Reddish brown.	Reddish brown.	Yellowish brown.	Brownish yellow.
Nitrophenol (para)	Colorless.	Colorless.	Colorless.	Colorless.
Rosolic acid	Yellow.	Yellow.	Yellow.	Yellow.
Litmus	Red.	Red.	Red.	Blue.
Lacmoid	Pink.	Pink.	Pink.	Pink.
Phenolphthalein	Colorless.	Colorless.	Colorless.	Colorless.
Tropaolin	Yellow.	Yellow.	Yellow.	Yellow.

Basic.

	$Ba(OH)_2$: OH-ions calculated in equivalent H-ions			
	$0.8 \cdot 10$	$2.0 \cdot 10^{-8}$	$9.0 \cdot 10^{-9}$	$7.0 \cdot 10^{10}$
Anilin violet	Violet.	Violet.	Violet.	Violet.
Anilin red	Yellowish red.	Red.	Red.	Red.
Anilin orange	Light reddish yellow.	Yellow.	Yellow.	Yellow.
Nitrophenol (para)	Deep yellow.	Deep yellow.	Deep yellow.	Deep yellow.
Rosolic acid	Orange.	Pale reddish yellow.	Red.	Red.
Litmus	Blue.	Blue.	Blue.	Blue.
Lacmoid	Blue.	Blue.	Blue.	Blue.
Phenolphthalein	Pale pink.	Light pink.	Pink.	Pink.
Tropaolin	Yellow.	Yellowish red.	Mahogany.	Mahogany.

In testing the blood for free H- or OH-ions, about 0.1 cc. of the indicator solution is measured out into a small vessel with a white background, 0.02 cc. of blood is added by means of the capillary hemometer pipet (see p. 744), and, after stirring, the change of color is noted. The specific color of blood will in no way hinder the carrying out of this process, as one can demonstrate by adding a solution of known ion content to the indicator solution. An hydroxyl ion-content of the blood, representing $2.0 \cdot 10^{-8}$ of hydrogen ions, would reveal itself, for instance, through column 6 of the tables, by showing a light tint with phenolphthalein and a yellowish brown with the tropaolin solution. Schultz has found in the insane cases examined by him no

[1] Monats. Psychiatrie und Neurologie, 1908, vol. xxii, Pt. 1.

noticeable changes in coloration of the indicators, which agrees with the opinion of Friedenthal and Höber, so that the blood from a physico-chemical standpoint may be considered as a neutral fluid, *i. e.*, it contains no free H- or OH-ions.

ESTIMATION OF THE COAGULATION TIME AND THE COAGULABILITY OF THE BLOOD

Coagulation Time.—The time elapsing before coagulation of blood occurs varies decidedly under pathologic conditions. It is difficult to give any constant normal figures, because coagulation depends so much upon external conditions, such as temperature, the shape of the vessel in which coagulation takes place, the amount of blood used, and the nature of the wound from which the blood is taken. This is the reason why so little is as yet known regarding pathologic variations.

H. Vierordt[1] recommends a method for determining the coagulation time of human blood which can be performed with very small amounts of blood and which appears to the author to be the most satisfactory for clinical purposes. The technic is as follows: A capillary glass tube, about 5 cm. long and 1 mm. in internal diameter, is filled with blood (by capillarity) for about one-half cm. From the other end there is introduced through the blood a white horsehair (about 10 cm. long), which has previously been carefully boiled with alcohol and ether, care being taken not to touch the end which comes in contact with the blood. To avoid warming, the capillary tube must be handled with Cornet forceps. Once every minute the hair is moved back and forth for ½ cm. through the column of blood. At first no blood sticks to it, but the moment coagulation begins the horsehair will show a reddish discoloration. As soon as coagulation is complete, the horsehair will appear white when pushed further into the tube, or the entire quantity of blood will adhere to it as a compact clot. In order to determine more accurately the length of time necessary for complete coagulation, it has been the author's custom to knot the posterior portion of the horsehair. At the moment of complete coagulation the entire coagulated blood-column may be drawn out of the tube as a compact mass when this knot is brought in contact with its posterior portion. Vierordt found the average time of coagulation with this method to be nine minutes. The author has found, however, that this is subject to extreme variations dependent upon the external temperature and the diameter of the capillary tube, so that the time of coagulation can be assumed to be pathologic only when it is compared with a control test in which normal blood is employed under exactly similar conditions.

A much simpler process for the determination of the coagulation time of the blood is given by Guiart and Gimbert.[2] Upon each of three slides which have been carefully cleaned in potassium hydroxid solution and then dried in alcohol and ether, is put a fresh drop of blood from the finger. The three slides are placed horizontally under a bell-jar, moistened inside to prevent evaporation, and are tested every minute by carefully tilting the slides and noticing whether the drop changes its form. Full coagulation has taken place at the time when the drop does not change its form with the slide in a vertical position. With this method the coagulation of normal blood generally requires about ten minutes. The blood can also be placed in a test-tube without moistening the slide, and one notes the time in which the drop of blood at the bottom of the tube begins to lose its motility and when the motility is entirely lost.

Wright places a measured quantity of blood in a number of capillary tubes, keeping them at a constant temperature (37° C. and 18½° C.), and estimates the time of coagulation by blowing out the tubes at regular intervals of time. At first he estimated the coagulation time from the absence of motion of the column of blood; now he estimates the coagulation point by blowing out the blood upon blotting-paper and demonstrating the clot.

The method of Russell and Brodie requires a complicated apparatus,[3] and depends upon the determination by the microscope of the loss of motility of the red blood-corpuscles caused by the coagulation. The most recent method for the estimation of the coagulation time is that of K. Bürker.[4] He places a drop of blood and a drop of

[1] Arch. der Heilk., 1878, vol. xix, p. 193.
[2] Précis de diagnostic chimique, 1906, Paris, Rudeval.
[3] Jour. Physiol., May, 1897.
[4] Pflüger's Arch., 1907, vol. cxviii, p. 452, and Verh. d. Cong. f. inn. Med., 1907, p. 515.

distilled water in the cavity of a hollow ground slide and sets it on a water-bath, especially constructed for his purpose, at a temperature of 25° C. This he touches lightly every half minute with a fine glass rod until the first thread of fibrin is caught up. The apparatus can be obtained from Albrecht, the mechanic of the University of Tübigen. The addition of water seems to the author to be questionable.

The time of coagulation is shortened by stasis, after transfusion, after hemorrhage, by hunger, and by the majority of diseases. The statement that the coagulation time of the blood is shortened when it is taken from an area of passive congestion is in marked contradiction to the fact that the blood in the corpse after suffocation is usually liquid. In the intervals between the hemorrhages of hemophilia the author has found the coagulation time to be markedly prolonged. During the hemorrhage, however, this coagulation time may be even shorter than that observed in normal blood. For further details in this connection the reader is referred to the author's article in the Zeitschrift für klinische Medicin, 1904–05, "Ueber das Wesen der Hämophilie."

PHYSICAL PROPERTIES AND CONTRACTILITY OF THE CLOT

A few cubic centimeters of blood obtained from a vein (see p. 730) are placed in a test-tube, and the behavior of the clot is observed. If coagulation be abnormally slow, the red corpuscles will be sedimented before coagulation is complete, and the upper layer of the clot then appears as a whitish, so-called "buffy coat." Great differences, which are not as yet quite satisfactorily explained, exist with reference to the rapidity and the completeness with which the clot loosens itself from the wall of the tube and contracts, with a resulting separation of the serum. According to Hayem and LeNoble, one observes a lack of contractility of the clot, independent of the rapidity of the coagulation, existing in grave infectious diseases, *e. g.*, pneumonia, in spite of normal or increased number of blood-plates, which, according to many writers, are responsible for the contractility of the clot, while in other cases (purpura, typhus, pernicious anemia, variola hæmorrhagica, and cachectic conditions of all sorts) the lack of contracting power is associated with a decrease in the number of blood-plates.

DETERMINATION OF THE HEMOGLOBIN IN THE BLOOD

A large number of methods have been recommended for use in this important part of blood diagnosis. The methods available for clinical purposes indicate only the relative amount of hemoglobin contained in the blood examined compared with the normal. Clinically, these relative values, expressed in percentages of the normal, are of primary interest. It is very easy to obtain from them absolute figures if the normal amount of hemoglobin contained in the blood be known. This is in a normal adult 13 to 14 gm. in 100 cc. of blood. As hemoglobin contains about 0.4 per cent. of iron, this would correspond to about 0.05 per cent. of iron content.

By the determination of the relative value of hemoglobin in percentage of the normal it was heretofore thought that the normal hemoglobin content maintained a constant and invariable value, and if this value were placed at a nominal 100, the relative hemoglobin value of any pathologic blood could easily be expressed in percentage of the normal. A blood which had, for example, only $\frac{4}{5}$ of the color value of normal blood would, according to this method of explanation, be considered as containing 80 per cent. of the normal amount of hemoglobin. The author has found by his new hemometer that the hemoglobin content under normal conditions may vary fully 20 per cent. Since this is so, these calculations in percentage of the normal can hardly be employed as formerly. With the exception of the spectrophotometric methods, which are too complicated for clinical use, the author's hemometer for the first time permits accurate and error-free colorimetric examinations. But it is not at all necessary to abandon the very convenient methods based upon these forms of calculation, although it must be borne in mind that the tables which one finds have only an empirical significance, the values of which each observer must establish for himself among his own group of patients, since he decides between which scale values he will limit the normal. (Compare the author's statement regarding his hemometer on p. 751 et seq.)

Leichtenstern found the following values for the hemoglobin content at the various ages, expressed in grams per 100 cc. of blood:

36 hours	19.329	3 years	10.971
2 days	21.160	4 "	11.341
3 "	20.451	5 "	11.151
4 "	19.488	6–10 years	11.796
8 "	17.869	11–15 "	11.701
10 "	17.129	16–20 "	13.034
14 "	16.124	21–25 "	13.870
3 weeks	15.023	26–30 "	14.727
4 "	15.362	31–35 "	15.013
10 "	14.293	36–40 "	14.685
12 "	13.828	41–45 "	14.420
14 "	14.388	46–50 "	12.494
20 "	12.928	51–55 "	12.696
½–1 year	11.373	56–60 "	13.150
2 years	11.151	Over 60 years	14.790

In this table a large number of observations were made on middle-aged and old people, and average figures were taken; but for the earlier periods of life only single observations were made. Nevertheless, the amount of hemoglobin contained in the blood in the first week of life is without doubt one-third larger than the average during the third and fourth decades. During the following weeks the quantity gradually diminishes, and remains one-fourth to one-fifth below the average from the second half of the first year to about puberty. From puberty to the forty-fifth year of life it remains about at the average, and then gradually diminishes. These figures correspond very closely to the variations in the number of blood-corpuscles, except that they are somewhat more striking. (See p. 763.)

The percentages upon clinical hemoglobinometers corresponding to these absolute values can be readily calculated from the above table if 13 to 14 gm. of hemoglobin in 100 cc. of blood be taken as 100 per cent. Stierlin[1] calculated these percentages, and found them to be as follows:

	Corrected percentage.[2]	
Newborn (1st to 3d day)	138.88	
½–5 years	76.58	78.44.
5–15 "	80.50	
15–25 "	88.88	
25–45 "	100.00	
45–60 "	87.50	

Miss Perlin, working with Fleischl-Miescher's hemoglobinometer under Stoos's direction, found the following percentages in children of different ages:

Age.	Corrected percentage. Minimum.	Maximum.
2 to 18 months	58	78
2 years	60	80
3 "	69	80
4 "	70	84
5 "	72	81
6 to 10 years	74	85
11 to 14 and 16 years	78	88

Hemoglobin determinations are of great value. Only since we have been able to determine the amount of hemoglobin have we recognized that an individual who is very pale need not necessarily be anemic, and that the pallor of the skin of the face may be due to lack of cutaneous transparency or to the fact that the skin contains only a very slight amount of blood. (See p. 38 et seq.) And only since we have been able to limit iron therapy to diseases where there is really a deficient amount of hemoglobin has it become rational therapy.

Clinically, the anemias (see Anemia) include those conditions in which there is deficient percentage of hemoglobin (oligochromemia), as well as hydremic plethora. (See p. 731.) Increased percentages of hemoglobin up to from 110 to 120 per cent.

[1] Blutkörperchenzählungen und Hämoglobinbestimmungen bei Kindern, Arch. f. klin. Med., 1889, vol. xlv.

[2] In regard to corrected percentage see p. 753 et seq.

are by no means uncommon in so-called full-blooded healthy individuals. (See Polycythemia.)

Numerous observations have established the fact that the hemoglobin percentage increases with increased altitude, just as does the number of blood-corpuscles. (Compare p. 764.)

ESTIMATION OF THE COLOR OF THE BLOOD FROM INSPECTION OF THE BLOOD DROP

One can form a fairly accurate opinion of the presence or absence of oligochromemia by simple inspection of a drop of blood from a finger prick. Pronounced chlorosis and marked pernicious anemia may be recognized by the strikingly pale, watery, and transparent hue of the blood.

TALQVIST'S HEMOGLOBIN SCALE

Talqvist has prepared a chromolithographic scale which corresponds to the shades given by a drop of blood caught on filter-paper according to the hemoglobin content. The gradations of the shades of the scale correspond to hemoglobin values differing from each other by 10 per cent. (normal being set at 100 per cent.). By this method, of course, only marked differences can be determined. It is nevertheless better than no attempt at blood examination.

GOWERS' HEMOGLOBINOMETER

This instrument (Fig. 296) consists of two glass tubes (*a* and *b*) about 11 cm. long and 0.8 cm. in diameter. One of them (*a*) contains 2 cc. of a standard picro-

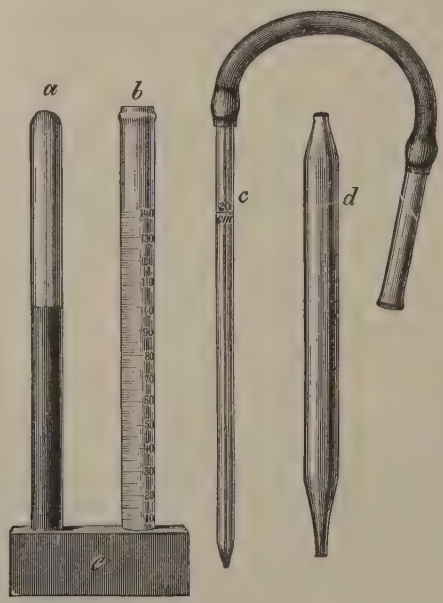


Fig. 296.—Gowers' hemoglobinometer (about two-thirds the natural size).

carmin solution, the shade of which corresponds as closely as possible to a 1 per cent. solution of normal blood. The other tube, closed at one end, is graduated so that

the level to which 2 cc. of fluid will reach corresponds to 100. If the calibers of the two be exactly alike, this will be exactly the level of the standard fluid in the other tube. Below the 100 mark the tube is subdivided into 100 equal parts, every ten of which are numbered. Each of these parts contain 20 c.mm. Both tubes can be held in a vertical position by setting them into a perforated rubber block (*e*). A capillary pipet (*c*) containing 20 c.mm., with a small rubber tube attached, is used for convenience in sucking up the blood. A non-graduated pipet (*d*) is used for making the appropriate dilution. It contains about 2 cc., and has an opening so small that water which has been sucked into it can only escape drop by drop.

The technic of estimating the amount of hemoglobin is as follows: Twenty c.mm. of blood are sucked up in the capillary pipet as quickly as possible, so as to avoid coagulation. The point of the pipet is wiped off, care being taken not to allow blood to escape from the lumen. Its contents are then quickly blown out into the graduated tube (*b*) partly filled with water. The blood and water are intimately mixed by stirring and by repeated sucking up and blowing out of the fluid. Tube *b* with the blood-mixture and tube *a* with the colored solution are now set up side by side in the rubber block. A thin piece of white tissue-paper is held behind the tubes, and their colors are compared by transmitted light. Water is added from the larger pipet, drop by drop, with repeated stirring, until the color in both tubes is as nearly alike as possible by transmitted light. The line to which the blood solution now reaches indicates at once the concentration of the hemoglobin, as the amount of water added to establish a definite shade of color is naturally proportional to the amount of hemoglobin contained in the quantity of blood used. Gowers acts upon the theory that the blood of a healthy individual has a certain definite and constant hemoglobin content, and the standard solution, therefore, is so prepared that the value 100 would obtain in a very large number of healthy people. But the author has proved that no such constancy of the normal hemoglobin content obtains (see p. 751), so that it is better to regard the scale as purely conventional and not to be deceived by the absolute value found. This instrument is accurate within 5 or 10 per cent., provided that the shade of the standard solution exactly corresponds to the color of blood. The disadvantages of the instrument are, first, that it is quite difficult to make the standard solution so that it will exactly match the color of normal blood, and, secondly, that its color will change after a certain length of time. A special standard solution must be used if the examination be made by artificial light. In view of these disadvantages, the author has constructed a new hemometer, in which some of the principles of Gowers' instrument are retained, and which will meet with the requirements of daily practice. The standard solution, however, is made up with blood-pigment instead of picrocarmin. (See p. 748 et seq.)

FLEISCHL'S HEMOMETER WITH MIESCHER'S IMPROVEMENTS[1]

Fig. 297 represents Fleischl's instrument for the clinical determination of hemoglobin with Miescher's improvements. The principle of the instrument is as follows: The stand is like that of a microscope. In the central opening of the objective stage is placed a cylindric chamber, divided into two parts by a vertical partition. This chamber (*M*) has a glass floor. One-half (*a*) is filled with a diluted solution of the blood to be examined. The other half is filled with water. A glass wedge stained magenta slides beneath the chamber by means of the screw T. R. The glass wedge and the chamber are illuminated from below by a plaster-of-Paris reflector P S. The colors in the two halves of the chamber are compared from above by transmitted light. The glass wedge is then adjusted until both sides of the chamber show the same shade, *i. e.*, until the portion of the glass wedge underneath the chamber filled with water has the color of the blood-solution to be examined. The position of the wedge is read off through the window (*m*) in percentage of hemoglobin. Artificial light must be employed—best a candle light. A white light is unsuitable, since by it the color of the wedge does not correspond to that of the blood solution.

The modifications of Fleischl's old apparatus, introduced by Miescher, are as follows: 1. The amount of blood employed can be much more accurately measured with the specially constructed pipet (mélangeur) than with Fleischl's former capillary tubes. 2. Blood of varying degrees of concentration can be compared with the aid of this mélangeur so that a control is kept of the individual examinations and of the

[1] To be obtained from C. Reichert, Optical Institute, Vienna.

evenness of the coloring of the glass wedge. 3. The scale of each instrument of the improved type is supplied with a caliber table of absolute hemoglobin values (in milligrams), whereas the scale of the old instrument showed the percentage of hemoglobin in relation to a more or less arbitrarily selected average. In this way many of the errors which with the old apparatus were due to the irregular coloring of the glass slide are avoided. 4. The chamber is covered with a glass (D) before attempting to read the percentage, and also with a diaphragm (Bl), so that the fields examined are sharply defined on all sides without any meniscus. 5. Two chambers of different depths are furnished with the apparatus so that the percentage of hemoglobin can be checked by comparing the two readings. 6. The coloring of the glass wedge has been technically improved, and is much more even than in Fleischl's original instrument.

The mixing pipet above mentioned (mélangeur) (Mel, Fig. 297) is made like a blood-counter. It consists of a capillary portion and a chamber 200 times the capacity of the former. The chamber contains a glass bead in the interior. A rubber tube is attached to the mélangeur. The drop of blood is obtained in the same way under the same precautions as for counting the blood-corpuscles. (See p. 754.) To dilute 200 times, blood is sucked up into the capillary portion to the mark 1,

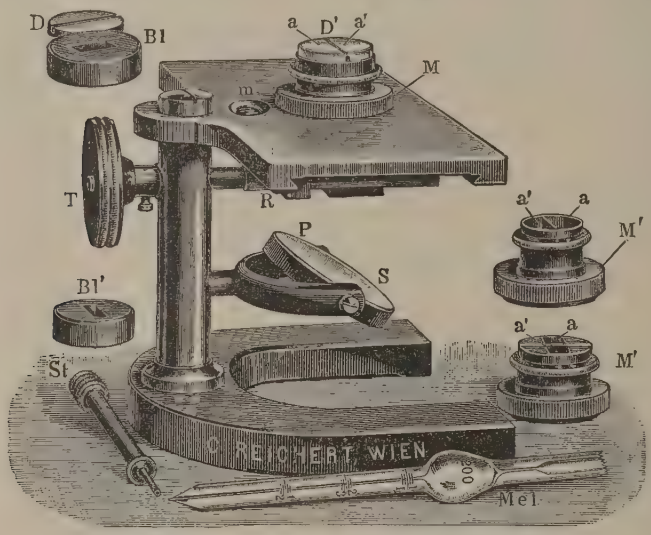


Fig. 297.—The new Fleischl-Miescher hemometer.

and then the diluting fluid (1 per cent. sodium carbonate solution), until the chamber is filled. It is then well shaken. To prevent air-bubbles which would render the dilution inaccurate it is well, while sucking up the diluting fluid, to hold the pipet vertically and to roll it gently between the fingers so that the glass bead will free any bubbles adherent to the sides. There are two other marks on the mixing pipet ($\frac{2}{3}$ and $\frac{1}{2}$), one of which corresponds to a dilution of the blood of 1 : 300, and the other of 1 : 400. If the blood cannot be sucked up readily enough to the desired mark, and there is danger of coagulation, the deficiency or excess in the quantity of blood may be determined by the small cross-lines above and below the main marks. Each of these accessory marks corresponds to the $\frac{1}{100}$ of the entire blood-column (up to 1), so that the excess or deficiency of aspirated blood may easily be deducted or added later.

For accurate comparison of the color shades, the solution of blood must be perfectly clear; otherwise the blood always seems somewhat darker than the color of the glass wedge. This is the reason that we employ a solution of soda, which does not quite dissolve the stroma of the blood-corpuscles, but renders it transparent. This soda solution must be reasonably fresh, as otherwise the blood will not appear perfectly clear, on account of the formation of bicarbonate of soda.

The details of technic in using the Fleischl-Miescher instrument for determining hemoglobin are clearly described in the directions accompanying the apparatus. They are copied from an article by Veillon, who demonstrated the reliability of the instrument.[1] Jaquet[2] claims from numerous experiments that the margin of error in the absolute quantity of hemoglobin determined by this instrument does not exceed 0.15 to 0.22 per cent. by weight of the blood, provided all precautions are taken. This instrument is, therefore, almost as accurate as the spectrophotometer, and is much simpler.

This is very likely true for certain individual Fleischl-Miescher instruments; but they are not uniform, for the color of the glass wedge in one corresponds more closely to the shade of the blood than does that in another. The author could not find a complete agreement with most of them, so that there has always been a great deal of uncertainty in their use. In addition, the coloring of the wedge in each instrument is by no means uniform. The author's assistants have also found that this instrument gives markedly different results with the same blood. Indeed, in view of the varying sensitiveness to color of individual observers, it could scarcely be otherwise, since they are not comparing identical, but merely similar, colors. In this respect the instrument is, therefore, always subject to an error in principle.

GRÜTZNER'S WEDGE HEMOMETER

This instrument, like the Fleischl-Miescher, depends upon the wedge principle. The blood dilution is placed in a narrow wedge-shaped trough, the sharp edge placed vertically below and the wide part, which is open, above. This trough is closed behind with ground glass, and in front with ordinary transparent glass. On looking through at various points of the wedge one naturally sees different shades on account of different thicknesses of the blood solution. The wedge as opposed to the Fleischl-Miescher instrument is stationary. A narrow gelatin plate, colored with picrocarmin, is placed as a standard next to the wedge and parallel with it, with its long axis vertical. In front of the wedge and the gelatin plate is a diaphragm which can be moved in the long axis of the wedge from its base to its apex. The diaphragm has three slits, somewhat more than 1 mm. broad, situated horizontally, parallel with the sharp border of the wedge, and extending over the wedge and the gelatin plate. The diaphragm is moved until one finds on the wedge that thickness at which the blood solution, seen through the middle slit by transmitted light, corresponds with the shade of the adjoining standard plate. The hemoglobin concentration in per cent. of normal can now be read off directly from the scale arranged on the diaphragm. A funnel of black, light-proof paper is used in looking through the slit to prevent interference by daylight. In order to obtain greater accuracy for paler specimens of blood there comes with the instrument a second standard plate which is of such a shade that the 100 point of the scale corresponds to 50 instead of 100 per cent. This instrument seems to have several advantages over the Fleischl-Miescher instrument. In particular, the color of the standard plate corresponds more accurately to the color of the blood than does the glass wedge of the Fleischl-Miescher instrument. The danger of a non-homogeneous coloration of the wedge is also eliminated. Only later observations can show whether or not the picrocarmin of the standard plate is permanent. With reference to the limited value of the percentage scale and the 100 value, see pp. 745 and 751 et seq.

[1] Arch. f. exp. Pathol. u. Pharmakol., 1897, vol. xxxix, p. 385.
[2] Correspondenzbl. f. Schweizer Aerzte, 1897, pp. 129 and 164.

HENOCH'S HEMATOSCOPE

This instrument depends upon the principle that, with a certain intensity of the blood color, or rather with a certain thickness of a slender column of blood, both known, absorption bands of oxyhemoglobin appear of equal width. (See Fig. 233, p. 545.) The apparatus consists essentially of two glass plates, slanting toward each other at an acute angle and thus inclosing a capillary wedge-shaped chamber. The undiluted blood from a finger-prick is allowed to flow into this chamber, thus furnishing a wedge-shaped, capillary blood column. Along the edge of this wedge a scale is attached containing 60 equal spaces, numbered from the base toward the apex of the wedge. The layer of blood is examined with transmitted light directly by means of a small hand spectroscope. (See Fig. 232, p. 544.) The latter is moved in the direction of the long axis of the wedge until both oxyhemoglobin bands are seen to be of equal width. One then observes the scale line which is opposite the slit of the spectroscope, and by its number obtains the absolute value of the hemoglobin content, *i. e.*, grains of hemoglobin in 100 cc. of blood. If one find, as, for instance, in normal blood, that the bands are equal at the line marked 14, which corresponds to a thickness of the wedge of 70 μ, one has then determined that the blood contains 14 per cent. by weight of hemoglobin. The test is easy, but the bands are not sharply defined, so that there is an opportunity for certain individual variations.

SAHLI'S NEW HEMOMETER

In the previously described clinical methods for the estimation of hemoglobin, which are those most commonly employed, the solution of blood is compared with an artificially colored substance, *i. e.*, either with a colored wedge of glass or with a solution of picrocarmin. To meet the demands of accurate colorimetry, however, the colored fluid to be examined should not be compared with a different substance, similar in color, but with a solution of known strength of the *same* coloring-matter. This is the only method by which the ability of the human eye to differentiate shades can be completely utilized. In addition to the great difficulty in obtaining an artificial standard color exactly like the color of the blood, whether it be by means of a glass wedge or a picrocarmin solution, the shades of the two colors will not coincide for all dilutions unless the standard color be made with the same substance as that contained in the fluid to be examined. This difficulty is quite apparent in any colorimetric appliance, such as the Fleischl-Miescher hemometer, in which different shades of the standard color must be compared with different concentrations of the blood to be examined. For analogous reasons, an artificial standard color can never be produced the shade of which will coincide with that of the blood both with natural and with artificial light.

The difficulty in applying this colorimetric principle lies in the fact that solutions of hemoglobin are not permanent. It consequently follows that if, in the interest of accuracy, we avoid employing artificial colors, we must utilize some permanent hemoglobin derivative in making the standard solution. The blood-solution to be examined is then converted into a solution of the same derivative, when a comparison may be accurately made. The application of this principle is limited practically by the necessity of employing only those derivatives of hemoglobin which may be produced in solutions of blood by simple chemical reactions.

After numerous attempts the author has succeeded in devising a method by which the hemoglobin of a solution of blood may be transformed into a derivative by quite a simple chemical reaction. With this derivative permanent standard solutions and colorimetric estimations may be made in accordance with accurate colorimetric principles.

The procedure consists simply in diluting the blood with 10 times its volume of $\frac{N}{10}$ hydrochloric acid. After a few seconds the fluid becomes dark brown from the formation of minute particles of hematin hydrochlorate.[1] Although this substance is not held in true solution, it has the same appearance, and when diluted with water forms a clear, brownish-yellow fluid, the pigment percentage of which may be colorimetrically determined by comparison with a permanent standard solution of the same substance.

The color comparison may be made by means of any of the colorimetric appliances, such as Hoppe-Seyler's colorimetric double pipet (see below). In the author's hemometer he has employed the same principle of comparison that is found in Gowers' instrument (see p. 744 et seq.), and which has proved to be so well adapted to the requirements of the practitioner. The standard hydrochloric acid solution, in a concentration corresponding to a 1 per cent. solution of normal blood, is sealed in a graduated glass tube. A similar accurately graduated tube, each division of which corresponds to 20 c.mm., is filled to the mark 10 with $\frac{N}{10}$ hydrochloric acid which has been saturated with chloroform to prevent the development of molds. With a capillary pipet like that employed in Gowers' instrument, 20 c.mm. of blood are introduced into the tube and well shaken. The mixture becomes practically clear and pure brown in color after the lapse of one minute,[2] water is added until the shade of the mixture exactly corresponds to that of the standard solution, when the hemoglobin percentage may be directly read off, as in Gowers' instrument.

In blood very deficient in hemoglobin, as in severe chlorosis or pernicious anemia, in which color equality is obtained upon the addition of water only to the line 15 or 20, the reading naturally will be relatively inaccurate, for one can scarcely graduate the addition of water under these circumstances, and make a reading with sufficient precision. In such cases three times the amount of blood should be employed, and the test performed as usual, and finally the hemometer reading should be divided by three. In this way, the same accuracy is obtained as with more concentrated blood.

The standard solution is only a suspension and not a true solution, so that a sediment forms after long disuse, and the tube must then be shaken. In the older instrument, this fault was corrected to a great extent by the use of glycerin as a diluent. But sedimentation still took place, and, as the suspension was restored only with the greatest difficulty, water has been used in the newer instrument for making the standard solution. A small glass bead, sealed in the tube, aids in stirring up the sediment. The author has kept the standard solution for a number of years without the slightest change in shade, and so ventures to assert that it is permanent, provided there be no error in its manufacture, such as a lack of asepsis. It once occurred that the stock solution was not well shaken up by the glass-blower, and so the tubes made from the upper portion of the fluid were too light a shade and those from the

[1] The substance produced is not methemoglobin, since the shade differs from that of methemoglobin formed in hemoglobin solutions by the addition of other acids. Its spectrum also differs from that of methemoglobin. The author has recently succeeded in producing Teichmann's hemin crystals from this fluid by extraction with acetic alcohol and subsequent evaporation.

[2] To obviate mistakes it is essential to wait as long as this.

lower too dark. The faulty tubes were replaced free of cost by the maker. The standard tube must be kept in the dark, for strong light can easily destroy the most stable substance.

The author has further improved this instrument, as compared with Gowers' (see Fig. 298), by placing the two tubes in a perforated black stand of hard rubber, which serves as a colorimetric screen. When the tubes are compared by transmitted light, the rays passing through the sides of the glass blend with the side light, and the colored surfaces are seen beside a black background. The stand is also provided with a ground-glass plate which diffuses the light before it reaches the tubes and obviates all disturbing reflections. By means of these appliances the optical impression obtained is that the fluid is contained in a small compartment with plane parallel sides. Such compartments are really necessary for accurate colorimetric estimations, in

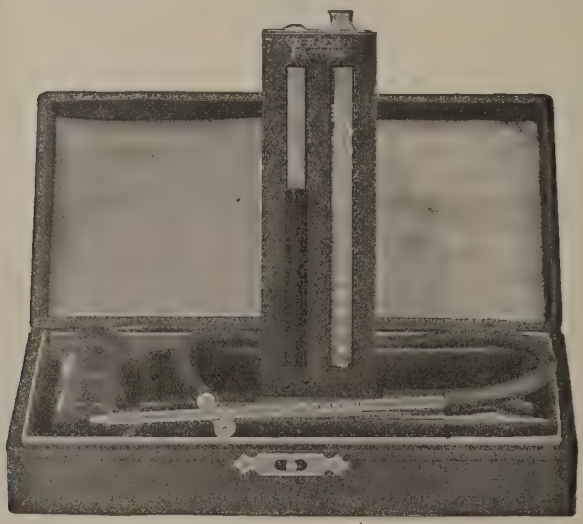


Fig. 298.—Sahli's new clinical hemometer.

order to compare completely homogeneous colored surfaces. They are very expensive, however, and not easily obtained in the small size necessary for the minute quantity of blood for examination. The appliance above described renders the employment of plane parallel glass vessels entirely superfluous, as may be demonstrated by the effect upon the eye. In addition to these improvements, the scale of the graduated tube may be turned completely behind the margin of the stand, so that it is not seen until the moment when the percentage is to be read. This has a twofold advantage in that the homogeneity of the colored surface is not disturbed by the scale, and that the investigator, in adding the diluting fluid, is not influenced by a preconceived opinion in reference to the expected percentage. The method may be made still more objective by covering all but the lowermost portion of the tube with black paper, so that the height of the fluid may not be seen at all.

The author has reached the conclusion that by means of these various contrivances, but chiefly on account of the absolute chemical and color congruity of the compared fluids, the simple hemometer devised by him, and made by the optician Büchi in Bern, gives as accurate results as the most exact methods of colorimetric examination of the blood, not excepting the more complicated ones. Furthermore, it is clear that the instrument must give the same result with both artificial and natural light, which is of the greatest advantage to the practitioner, who must work under the most varied conditions. The most accurate result will possibly be obtained in a dark room with artificial light, since under these conditions the eye is the most sensitive to light and color; but even with daylight the results are quite exact. The procedure is practically as simple as with Gowers' instrument.

The author would finally call attention to the fact, which he has directly proved experimentally, and upon this the entire procedure is based, that the brownish-yellow color produced by the addition of hydrochloric acid and subsequent dilution with water is directly proportional to the hemoglobin percentage of the blood examined. In other words, the accuracy of the colorimetric dilution method is not impaired by a dissociation of the hematin hydrochlorid combination which is formed.

REMARKS ON THE STANDARDIZATION OF THE SAHLI HEMOMETER

The author started with the principle employed in the older instruments, all of which, to the present date, are based on the assumption that the blood of a normal person has a constant color intensity, and for this reason the standard solution, as in all other instruments, was so made that normal blood, prepared according to the above-described method, showed, on the addition of water to the 100 mark, the same shade as the standard solution. Normal blood should, therefore, with this instrument give a hemoglobin value of 100 per cent. Experience with the very sensitive and exact new hemometer has, however, convinced the author that such an absolute normal point does not exist, but that in a perfectly healthy individual the normal percentage figures may vary fully 20 per cent. This important fact was not recognized earlier, because with the older colorimetric instruments, made with artificial dyes, the blood solution showed merely great similarity to the standard, but never a perfect color equality. Such physiologic variations of the hemoglobin content of the blood may deprive hemoglobin estimations of some of their value (independent of the determination of the variations in the same individual) if the differences found are not greater than those that may normally appear. Nevertheless, the use of an apparatus which designates the normal as 100 appears problematic, although an average could be obtained from a great number of estimations on healthy individuals, and the standard solution so made that this average corresponded to the 100 point on the hemometer scale. The author has refrained from this procedure in the newer instrument for the following reasons: He has learned by experience that color comparison with saturated color shades is more accurate than with the lighter shades for physiologic optical reasons. Chiefly on this account, in the newer instrument, not the *average* of the very variable normal point, but the *maximum* normal point found, is designated 100. The solution which is, therefore, darker than in the former instrument is so prepared that only his healthiest young assistants actually reach the 100 point.

The majority of individuals show lower values—men, such values as 80, 85, or 90. In other words, the normal point in healthy men varies between 80 and 100 with the newer instrument. Among women the normal values are about 10 points lower, so that one can consider the normal value in women between 70 and 90; and, in fact, the values standing near the lower grade predominate. This change of the instrument will, indeed, seem strange to those who still believe that the hemoglobin content of normal blood is a fixed quantity, but the author believes that it is warranted by facts and that one soon becomes accustomed to it. Were it only necessary to make the shade, which is used for comparison, darker, with the retention of the normal average as 100, this could only have been accomplished by increasing the caliber of the tube. But this would require another instrument, and it is naturally a good policy not to alter an instrument again constructively. On this account, there remained no other alternative than to make the solution more concentrated, so that 100 corresponds to the maximal normal value. The author confined himself to this improvement, requiring no constructive change, even more readily, as thereby that very important and fictitious idea of the constancy of the normal hemoglobin content of human blood would be best opposed. This false idea is responsible for the fact that too many cases of chlorosis are diagnosed, and, at the same time, many very important changes, as incipient pulmonary tuberculosis, are overlooked. With reference to this, see the dissertation of Frl. Dubnikoff,[1] prepared, at the author's suggestion, under the direction of Dr. Seiler, which plainly demonstrates that the hemoglobin values at the lower normal limits (70 in women) show an increase with the administration of iron, at the same time with an improvement of symptoms, and they, therefore, belong to the class which the author has named "masked chlorosis."

Since the hemoglobin value of normal blood varies fully 20 per cent., and since it is influenced by the altitude at which the individual in question lives, and perhaps also by the race, the nutrition, and many other factors, it is necessary that every observer should determine from his practical experience the lowest percentage value which he considers normal, and thereby the value below which he would diagnose an anemia. One must remember, too, the fact that the scale of a clinical hemometer has not, as was formerly thought, an absolute, but merely an empirical, value. For this reason the writers of scientific publications on hemoglobin estimation should be required to state the hemoglobin value which they consider normal for their method of procedure and the instrument used. (Compare Corrected Hemoglobin Percentage, p. 753, etc.)

An observer who possesses a standard tube, which, for some reason or other, does not show a perfect shade, will still be able to undertake accurate estimations with the instrument, for he can correct his tube by means of a number of observations upon a number of healthy individuals, thus finding the limit of the normal value on his instrument, and then easily make the calculation to determine the value which a perfect instrument would give. If, for instance, he find the lowest normal value in a healthy man to be 90 instead of 80, he determines the value which a perfect instrument would give by multiplying the percentage found by $\frac{8}{9}$. In a similar way, one can easily calculate values

[1] Dubnikoff, Clinical Investigation on the Action of Iron and "Marked Chlorosis," I. A. D., 1908.

by correcting the tube used with one that does not agree accurately with it in color. This case arises when an originally faulty or spoiled tube is replaced by a new and accurate one. The hemoglobin content of the blood in question is determined, first with the old and then with the new tube. If, for instance, it be found that the old tube shows 90 and the new tube 80, the old value must be multiplied by $\frac{8}{9}$, in order to correct it for the new instrument, and, on the contrary, with $\frac{9}{8}$ if one wishes to reckon new values on the old instrument.

Since there is a variation in the hemoglobin content of the blood of fully 20 per cent., under normal conditions, it is logical to demand that the percentage calculation of the hemoglobin in the sense of percentage of the normal be abolished. Such means of calculation can be properly employed when there is a fixed normal point. It would be very desirable indeed to gauge the hemometer on the absolute hemoglobin value, *i. e.*, grams of hemoglobin in 100 cc. of blood. The author would have undertaken this change long ago if it were not beset with peculiar difficulties, which depend on the fact that the hemoglobin of various preparations, themselves in a crystalline state, apparently possess different color values on account of the varying water content, so that it is very difficult to state positively that the hemoglobin used for a calibration is perfectly pure; another difficulty is the fact that, since the hemoglobin of the various species of animals varies, one naturally must employ a pure human hemoglobin in order to gauge absolutely the hemometer to be used for estimations on man, and this necessitates large quantities of blood. For these reasons the author has not as yet undertaken any work on these lines, but intends, however, as soon as time permits, to gauge the standard solution spectrophotometrically upon a definite "extinction coefficient" of the corresponding blood solution, so that then, according to the spectrophotometric investigations of Hüfner and others occurring in the literature, we shall be able to calculate absolute hemoglobin values from the hemometer scale readings.

METHOD FOR CORRECTING THE HEMOGLOBIN PER CENT.

If one wish, in spite of the difficulties described, to retain the statement of the hemoglobin value in percentage, he must rereckon the numbers read off directly from the hemometer as percentage of the normal, because such numbers, which one should consider simply hemometer numbers, are indefinite and serve merely to lessen the misunderstanding. The author proposes that the percentage numbers so calculated be designated "corrected percentage." If an observer in a given case find, by means of his hemometer, an amount of hemoglobin equal to 70, while he normally finds by this means an average amount equal to 80, the corrected percentage value of the given blood will be $\frac{70}{80} \cdot 100 = 87$ corrected percentage. If the hemometer in question give an average value in women equal to 70, then a hemometer reading of 70 gives a corrected percentage value of $\frac{70}{70} \cdot 100 = 100$ corrected percentage. As one can see, the corrected percentage value of equal shades for the two sexes comes out differently, and this fact must naturally be remembered in the calculation of the color index (p. 765).

THE HEMATOSPECTROPHOTOMETER

The most accurate method of determining the amount of hemoglobin is by means of the spectrophotometer, first used by Vierordt and perfected by Hüfner.

This instrument, however, is much too complicated and too expensive for practical purposes, so that the author will refer for a description to Hüfner's essay in the third volume of the Zeitschrift für physiologische Chemie, p. 562, and to Krüss' work, Colorimetrie und quantitative Spectralanalyse, Hamburg und Leipzig, Leop. Voss, 1891.

THE HOPPE-SEYLER COLORIMETRIC DOUBLE PIPET

This very excellent apparatus is also too complicated for clinical purposes.[1]

THE COUNTING OF BLOOD-CORPUSCLES

THE COUNTING OF RED BLOOD-CORPUSCLES (Erythrocytes)

It is almost impossible to form any idea of the number of red blood-corpuscles contained in the blood by simply inspecting a microscopic preparation, unless the number is so greatly diminished that the preparation shows few or no rouleaux. Actual counting is the only proper procedure. Numerous methods of counting have been advocated. In all of them a known quantity of blood is diluted to a definite proportion with a solution which preserves the red blood-corpuscles, and then those contained in a definitely measured space are counted. The number of red blood-corpuscles in 1 c.mm. of undiluted blood can then easily be calculated by simple multiplication.

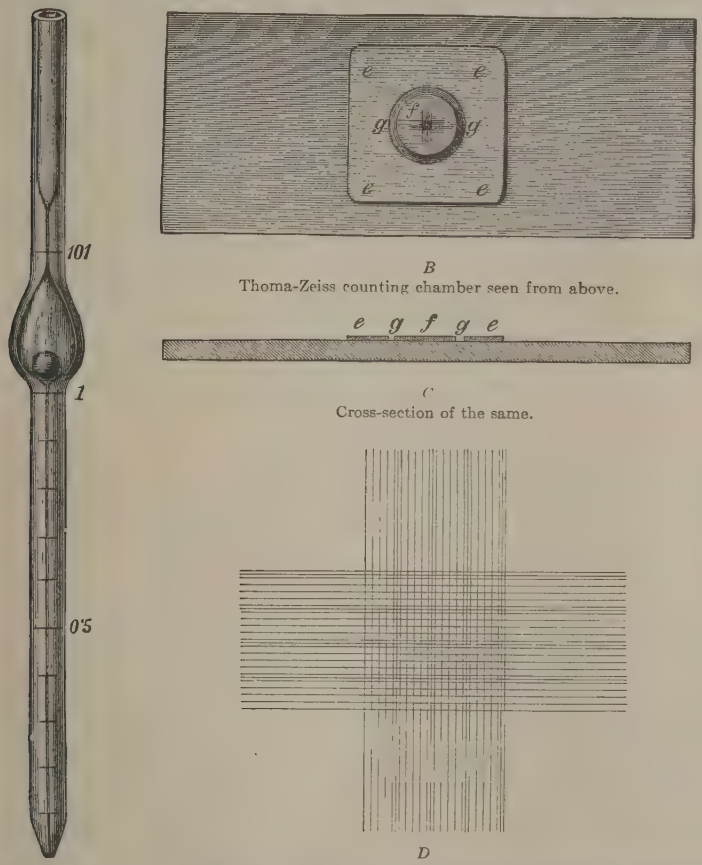
The simplest and most practical blood-counting apparatus is that constructed by Thoma and Zeiss (Fig. 299). It is based upon the older principles of Malassez, Hayem, and Gowers. It consists of two parts, a counting-chamber upon a slide, and a mélangeur. The latter consists of a capillary pipet with an ampulla containing a freely movable glass bead. As is shown in the figure, the mélangeur is so constructed that the ampulla contains 100 times the cubic contents of the capillary tube. A rubber tube is attached to the upper end for convenience in sucking up the blood.

The counting-chamber is represented in Fig. 299, *B*, from above and *C*, in section. Two plane glass plates are cemented to a slide. The smaller (*f*) is circular; the larger (*e, e, e, e*) is square, somewhat thicker than *f*, and with a circular opening in the center, in which *f* is centered, leaving between the two a circular moat (*g*). The floor of the moat is formed by the slide itself. The upper surface of *f* is exactly 0.1 mm. below that of *e* (not shown in the cut). In the center of *f*, which forms the floor of the counting-chamber, 1 sq. mm. of the glass is ruled with a microscopic scale into 400 (20 × 20) squares (Fig. 299, *D*, formed by two series of lines which intersect at right angles). Each square has a surface of $\frac{1}{400}$ sq. mm., each side being $\frac{1}{20}$ mm. Breuer's chamber (see Fig. 301, p. 758), originally devised for counting the leukocytes, may also be used for the red cells. This chamber is covered with a carefully ground cover-glass, made thick enough not to bend. The chamber is therefore, divided into little square prisms, each one of which has a cubic conten of $\frac{1}{4000}$ c.mm. This fraction forms the basis of subsequent calculations. The chamber is very carefully ground, and to avoid error the cover-slip should rest very accurately upon the slide. It is carefully pressed down upon the square glass *e, e, e, e*, until the "Newton's rings" which are produced remain permanently (*i. e.*, after the pressure has been removed), merely from the adhesion between the cover-slip and the margin of the chamber. The moat (*g, g*) around the glass (*f*) prevents the blood-mixture upon *f* from running in between the cover-slip and the square glass (*e, e, e, e*), and so altering the depth of the chamber. For the counting of white blood-corpuscles, which, for sake of accuracy, demand a larger surface, the Thoma-Zeiss chamber has been variously modified in its divisions. The most important of these, useful also for the enumeration of the red blood-corpuscles, will be described in the section on the Counting of Leukocytes. (See p. 757 et seq.)

The method of procedure is as follows: In extracting the blood we must avoid any pressure in the vicinity of the puncture, otherwise congestion or lymph exudation may make the results inaccurate. The blood is sucked up into the capillary tube to the mark 1; the ampulla is then filled up to the mark 101 with a 3 per cent.

[1] Zeit. f. physiol. Chem., 1892, vol. xvi, p. 505, and Lehrb. der physiol.-chem. Analyse, 1893, p. 414.

solution of sodium chlorid or a 5 per cent. solution of Glauber's salts, or, better still, Hayem's fluid.[1] While sucking up the diluting fluid, the mélangeur should be held vertically and rotated slightly to whirl the glass pearl a little, and dislodge any adherent air-bubbles which would make the degree of dilution inaccurate. A 1 : 100 dilution of the blood is thus prepared for counting. After thorough shaking (the author demands five minutes), 2 or 3 drops of the fluid are first blown out, the point of the pipet is wiped off, and a small drop of the solution is carefully placed upon the center of the counting-chamber, *i. e.*, over the ruled scale. The cover-glass is



A
Mélangeur.

B
Thoma-Zeiss counting chamber seen from above.

C
Cross-section of the same.

D
The ruling upon the new Thoma-Zeiss slide, enlarged 20 times. 1 sq. mm. of the figure = $\frac{1}{400}$ sq. mm. The large central square has an area of 1 sq. mm.

Fig. 299.—Thoma-Zeiss blood-corpuscle counting apparatus.

immediately adjusted before the corpuscles can sink, and pressed down at the margin until Newton's rings appear. If these do not remain after removal of the pressure, the preparation must be made over again. The chamber and cover-glass must then be still more carefully cleansed, for the trouble is usually due to dust getting between the margin of the chamber and the cover-glass.

[1] Hayem's fluid: Sublimate, 0.5; sodium sulphate, 5; sodium chlorid, 2; aquæ destillatæ, 200. This also preserves the red color of the cells, and facilitates a distinction between the red and the white blood-corpuscles.

The mixing pipet frequently causes a great deal of trouble: either the fluid flows out of the capillary part too soon, or, on the contrary, it is drawn into the narrow part of the tube above the ampulla, or even into the rubber tube during aspiration, thus destroying the accuracy of the dilution. Therefore, the author has recently preferred to perform the mixing without the mélangeur, as follows: The required amount of the diluent is measured into a small glass by means of a pipet, which must be carefully dried on the outside after the fluid is drawn in. The required amount of blood from a capillary pipet is then added, and the mixture stirred rapidly for at least five minutes with a slender glass rod. In adding the blood to the diluent the capillary pipet must be thoroughly rinsed with the diluting fluid, by drawing it in and blowing it out several times. The pipet used for the diluent must also be rinsed with the mixed solution, in order to clear out any of the diluent that may adhere to its interior. We then place a drop of the solution, by means of a pipet or dry glass rod, on the counting-chamber, and cover it immediately with a cover-glass before the corpuscles sink. This is the mixing apparatus that Hayem has recommended. It is made by Nachet, 17 Rue St. Severin, Paris, but can be prepared by any glass-blower. The pipet for measuring the diluent is graduated for $\frac{1}{4}$ and $\frac{1}{2}$ cc. The two capillary pipets for measuring the blood are graduated as follows: 2, $2\frac{1}{2}$, 3, 4, 5 c.mm. for the red corpuscles, and 5, 10, 15, 20, 25 c.mm. for the white blood-corpuscles. The slide is allowed to remain horizontal for about a minute after the cover-slip is in place, until the blood-corpuscles have settled to the bottom of the chamber, and then the corpuscles are counted. For greater accuracy two counting-chambers may be prepared, and compared to be sure that the blood-corpuscles are about evenly

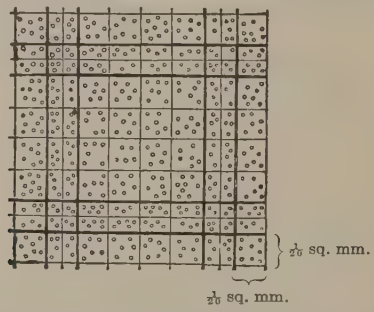


Fig. 300.—Microscopic picture of a part of the ruled surface of the Thoma-Zeiss chamber with blood-corpuscles upon it (high power). The central square bounded by double lines corresponds to the "quadrille" of the Hayem-Nachet chamber (see Fig. 304, p. 762), and has an area of $\frac{1}{25}$ sq. mm.

distributed in each. If this be not the case, fresh preparations should be made after repeatedly shaking the mélangeur. A medium power is the best for counting; for instance, a Leitz No. 5 or a Zeiss C or D objective. Fig. 300 shows the appearance of the red cells in a series of squares.

In the modern apparatus each fourth and fifth division line of the chamber is more heavily ruled, and an extra line is ruled halfway between them (Fig. 299, *D*, and Fig. 300).

For an *approximate count*, each series of 4 squares in a row, which is thus marked off, may be taken as a unit, the procedure being as follows: When the cells in such a series are counted, a memorandum of the number is made, and the average of a large number is multiplied by 100,000 in order to obtain the number per cubic millimeter. Since, if one small square equal $\frac{1}{10} \times \frac{1}{400}$ c.mm., 4 equal $\frac{1}{1000}$ c.mm., and, since the blood has been diluted 100 times, the factor is 100,000. To avoid counting any cell twice, cells touching the upper and left boundaries of any square are counted in that square; those touching the lower and right sides are excluded.

For *accurate counting* a mechanical stage should be used, and a large number of horizontal rows (20 squares each) counted.

The result is, naturally, more exact the greater the number of squares counted. According to Reinert, the error in counting 200 squares is about 3 per cent. It is, therefore, best to count 400 squares, and multiply the result by 1000 to obtain the number per cubic millimeter.

To determine the number of cells contained in 1 c.mm. of blood we divide the number of cells counted by the number of squares; the resulting quotient is

the number of cells in one square; this we multiply by the dilution, and divide by the size of the tiny prism. Suppose, for example, that in counting 100 squares we find 980 cells.

$$\text{Number of cells,} \quad \frac{980}{\text{Number of squares, } 100} \times 100 \text{ (the dilution)} \times 4000 = 3{,}820{,}000$$

The size of each tiny square prism is marked upon the counting-slide, and so need not be memorized.

Unless there is a decided diminution of red cells (anemia), it is easier to count a preparation diluted 200 times. For such a dilution we suck up blood to the first mark 0.5, and then suck the diluting fluid to the 101 mark (just above the bulb). Some examiners find that a sliding stage makes counting easier and more accurate. The more cells we count, the more accurate our result.

If, however, we deal with very marked anemias, with very great decrease of the blood-corpuscles, the usual method of counting will be less accurate than ordinarily, as the absolute number of the counted corpuscles will be less. It is better in such cases to dilute the blood less in preparing the counting mixture. This can be done by using the mixing pipet ordinarily employed for leukocytes. This makes possible a dilution of only 1 in 10 to 1 in 100. (See note 2.) The Nachet apparatus (see p. 756) is also well adapted for counting such weak dilutions.

In the above-the fact that the blood contains white as well as red cells has been disregarded. The former should properly not be counted. It is, however, difficult to differentiate them with moderate magnification. Except in cases of leukemia and marked leukocytosis there is no disadvantage in counting all the cells as erythrocytes, since the number of white cells is relatively very small. In cases where the number of leukocytes is too large to be disregarded (*e. g.*, in leukemia and marked leukocytosis) it is best to count all the cells, and then subtract the number of leukocytes determined by methods described below.

In regard to the innovations introduced in Bürker's counting-chamber, see p. 759 et seq.

THE COUNTING OF THE WHITE BLOOD-CORPUSCLES (Leukocytes)

It is very difficult to judge the number of leukocytes in a specimen of undiluted blood, because they are usually distributed very irregularly and often seem to be hidden or jammed in between the rouleaux of the red blood-corpuscles. For this reason we dilute the blood, and count them as explained in the following:

Two conditions must be fulfilled: first, the leukocytes must be made easily recognizable with the rather low power used in counting; and, second, considerably larger amounts of blood must be used than in counting red blood-corpuscles, because the number of leukocytes is so small (unless, of course, they are very considerably increased—leukemia). These conditions are best fulfilled by Thoma's[1] method as follows: The blood is diluted with a ⅓ per cent. aqueous solution of acetic acid. Türk uses a 1 per cent. solution of acetic acid and adds gentian-violet (1 : 6000) to stain the nuclei. The acid dissolves the red blood-corpuscles, leaving leukocytes clearly visible. A special mélangeur is used; its bulb contains only 10 times as much fluid as the capillary tube.[2] Instead of this the dilution may be

[1] Counting the white blood-corpuscles in the same preparation with the red is not advisable, since the absolute number of leukocytes is too small after the high dilution necessary for red blood-corpuscle counting. If, despite this disadvantage, combined counting be attempted (for merely approximate determinations), the leukocytes must be stained in order to distinguish them from the red cells. This may be done, however, by using, in a 1 : 100 dilution, the following mixture proposed by Toisson: Aq. destil., 160; glycerin neut. (30° B), 30.0; sodium sulphate, 8.0; sodium chlorate, 1.0; methyl-violet 5 B, 25 mg. There is also recommended, as a diluent (1 : 100 dilution), a 3 per cent. NaCl solution with the addition of $\frac{1}{100{,}000}$ gentian-violet.

[2] Recently Zeiss has added to his blood-corpuscle counting apparatus a second pipet for leukocytes. In order to use this for the preparation of dilutions from 1 : 10 to 1 : 100, as desired, the capillary portion of the pipet has been marked off into subdivisions. This pipet can also be used for the counting of red blood-cells in cases of marked anemia.

made with Hayem's instruments. These have a great advantage over the mélangeur in that, owing to the larger bore of the latter, the fluid very readily runs out. In marked leukemia a dilution of 1 : 100 or even 1 : 200 may be used. After preparing the mixture, the technic is very similar to that for counting red cells (p. 755). It is advantageous, however, to employ a larger counting-chamber, such as those devised by Zappert, Elzholz, Türk, and B. Breuer. On account of its clearness, Breuer's chamber seems best. Fig. 301 shows how it is divided.[1] The depth of this chamber is 0.1 mm. The middle, finely ruled portion corresponds exactly to the original Thoma-Zeiss chamber (Fig. 299, p. 755) and is used for counting red cells. For counting leukocytes the long rectangles serve as counting units, unless one prefers to count through the entire chamber with a mechanical stage. The total ruled area of Breuer's chamber is 9 sq. mm., that of one long rectangle $\frac{9}{36} = \frac{1}{4}$ sq. mm. The central part, corresponding to Thoma's chamber, is 1 sq. mm.; the little squares (1 mm. square in the figure) actually measure $\frac{1}{20}$ mm. on each side, and have an area of $\frac{1}{400}$ sq. mm. The division of Türk's counting-chamber is also very practical.[2] With this large chamber a great number of leukocytes may be rapidly counted, and so greater accuracy secured (see below). After the drop of diluted blood has been placed upon the floor of the counting chamber, it should be examined with a low power, so that the examiner may convince himself that the leukocytes have been evenly distributed. Just as in counting erythrocytes, it is best to employ two

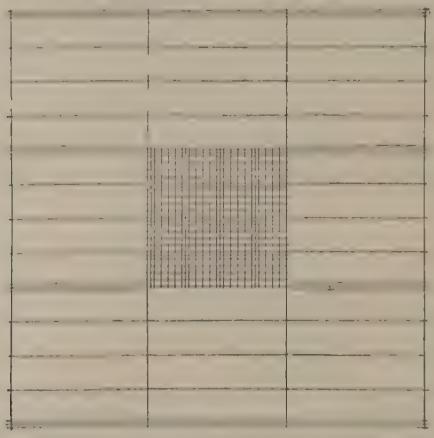


Fig. 301.—Ruling of Breuer's counting chamber. Enlarged 20 diameters, as in Fig. 299. 1 sq. mm. in the figure = $\frac{1}{400}$ sq. mm. The whole figure has an actual area of 9 sq. mm. Each large square = 1 sq. mm.

counting-chambers at the same time, and to be sure that the leukocytes are present in about the same proportions in both chambers.

Türk recommends counting at least 300 to 1000 leukocytes. This is very easy if Elzholz's, Zappert's, Breuer's, or Türk's chamber be used. If the dilution be 1 : 10, and the leukocytes normal or increased in number, 5 sq. mm. should be counted; in leukopenia, 9 sq. mm. In the latter case the number of cells counted, multiplied by $\frac{100}{9}$, gives the number per cubic millimeter. Reinert found that the probable error was 3.6 per cent. one way or the other, even when 4000 cells were counted. If only approximate counts be wanted, the large rectangles of the Breuer chamber (Fig. 301) can be used as units. We then count the contents of several of these rectangles, and multiply the average (in a 1 : 10 dilution) by 400, in order to find the number of leukocytes in 1 c.mm., or we may use as a unit the medium-sized square, situated in the large central square of the Breuer chamber (Fig. 301), which is included within the double lines, and consists of 16 of the smallest squares. It, therefore, represents an area of $\frac{16}{400} = \frac{1}{25}$ sq. mm. and a capacity of $\frac{1}{250}$ c.mm. In a dilution of 1 : 10 it is, therefore, necessary to multiply the average count by

[1] Made by Zeiss in Jena, described in Berlin. klin. Woch., 1902, No. 141, p. 954.

[2] Türk, Vorlesungen über klinische Hämatologie, W. Braumüller, Vienna and Leipzig, 1904, p. 95.

2500, in order to obtain the number of leukocytes in 1 c.mm. of blood. This square has the same capacity as the large squares of the Hayem counting-chamber (Fig. 304).

With reference to Bürker's modification of the counting-chamber, see below.

In pathologic cases the count should, if possible, be taken just before a meal, *i. e.*, at a time to avoid the leukocytosis of digestion. The leukocytosis of digestion is almost always absent if very small and frequent meals of fatty and starchy food be taken (Rieder).

The counting of the various kinds of leukocytes (differential count) is best done in stained dry smears. (See p. 794 et seq.) It may be remarked, however, that by the use of certain colored diluents (see Chamber Coloring, by Zollikofer and by Turk, p. 795 et seq.) we may, to a limited extent, make a differential count in the counting-chamber.

In regard to the normal, total, and differential leukocyte count, see pp. 763 and 788 et seq.

BÜRKER'S COUNTING-CHAMBER

While the different counting-chambers, mentioned on p. 757, vary only in the manner of the ruling, K. Bürker[1] has constructed a counting-chamber which varies in principle from the former, since it is filled by allowing the dilution to be counted to flow by capillarity into the chamber, under the edge of the previously applied cover-glass. This method had been previously employed by Afferow,[2] but it had never received any general recognition. Bürker believes that in this way he obtains a more uniform distribution of the corpuscles in the chamber than is possible with the older

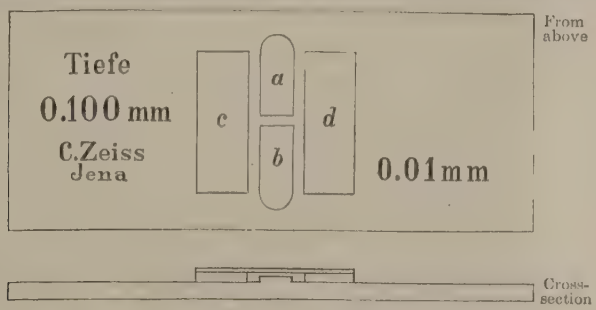


Fig. 302.—Bürker's counting chamber without the positioning clamps.

forms. He has proved to his satisfaction that, with the older methods, even if only a minute interval of time elapse between the placing of the drop of blood dilution and the application of the cover-glass, the corpuscles sink quickly, and, upon applying the cover-glass, an almost corpuscle-free solution will be drawn to the periphery of the counting surface, and the corpuscles will be piled up just where the rulings on the counting surface are found. For this reason, the Bürker chamber is made open at the sides. Bürker sees in this the further advantage that the chamber is totally unaffected by the atmospheric pressure, which he has found can influence the depth of the chamber on account of the air-tight sealing of the chamber. This is not of any importance in the ordinary examination, but is of great importance where there is wide atmospheric pressure variation, as in the examinations conducted in pneumatic chambers, in balloon ascensions, etc.

The Bürker chamber is schematically represented in Fig. 302. *a* and *b* are the two counting surfaces, separated by a transverse groove, and each of them has a lattice-work ruling. This double counting surface allows one to make, without interruption, two successive controlling counts from the same blood dilution. *c* and *d* are the supporting surfaces for the cover-glass. (See the profile view of the apparatus in Fig. 302.) Before putting in the fluid to be counted the cover-glass is so applied that the Newton rings over *c* and *d* are visible. In the newer apparatus there is a contrivance, not shown in the above figure, by which the cover-glass is held down on *c* and *d* by means of two metal clips, fixed into holes in the foundation plate of the

[1] Pflüger's Arch., 1905, vol. cvii, p. 426, and ibid., vol. cxviii, p. 460.
[2] Arch. de Physiol. norm. et Path., 1884.

chamber. The semicircular projections of *a* and *b* serve for the filling of the chamber, for the blood dilution from the mixing pipet when placed upon them flows by capillarity under the cover-glass. After filling the chamber with the blood dilution one should let it rest on a horizontal plane for at least three minutes, and then determine, by the following method, whether or not the corpuscles are evenly distributed. For the red blood-corpuscles it is better, according to Bürker, to examine the counting-chamber, not with a low magnification, as this gives too small an area, but with the naked eye, after placing the chamber on the stage of the microscope and lighting up its surface from below through the widely open diaphragm. If the distribution be uniform, we observe a general clouding, while an unequal distribution is noted by an unequal clouding. For the white corpuscles, however, one recognizes a uniform distribution by glancing over the counting surface with a low magnification. Fig. 303 shows the Bürker rulings. Bürker counts by means of a movable stage, or, in the absence of this, he moves the counting-chamber on underlying millimeter-ruled paper. Unlike the usual method, he does not count consecutively, but by individual squares, which serve as the unit. These, as shown in the diagram, are separated from one another. Besides this, just as in other forms of counting-chambers, there is a modification in which the counting surface is unruled, and the counting is accomplished by means of three ocular diaphragms of different sizes.

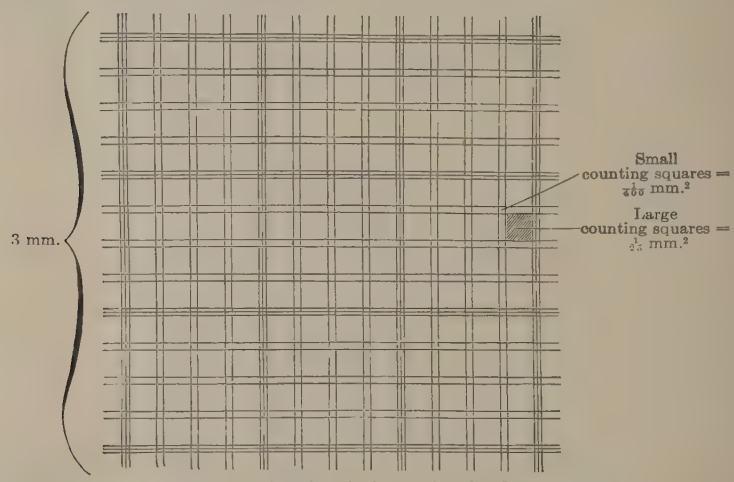


Fig. 303.—Ruling of Bürker's counting-chamber.

By means of a micrometer network, engraved on the base plate at the side of the chamber, these diaphragms are regulated by lengthening or shortening the tube of the microscope, so that they represent areas upon the floor of the chamber of $\frac{1}{400}$, $\frac{1}{250}$, and $\frac{1}{25}$ sq. mm. This modification has the advantage that the blood-corpuscles do not stick in the grooves of the ruling, and the counting can be carried out, as with the Nachet instrument (see below), with less attention and care. The disadvantage is that the diaphragms must always be regulated whenever an objective or ocular is changed. If, however, one always use the same lens, the length of the tube may be adjusted once for all, and the area seen through the diaphragm is, therefore, constant. This method seems to the author to be especially serviceable when only one observer uses the microscope, while at a clinic, where several assistants must use it, the diaphragm apparatus allows too many mistakes. Bürker has found that with his chamber, counting 80 small squares gives just as accurate results as counting 200 squares of the older chambers. This he attributes to a more uniform distribution of the corpuscles. He found, in comparative counting of the red blood-corpuscles, a variation merely of from 0.0 to +0.6 per cent. In using the ruled chamber the squares designated in the figure as "small" serve as counting units for the red blood-corpuscles, while the ones designated "large" are used for the white corpuscles. As a practical rule for calculation, Bürker suggests that, in order to find the number of red blood-corpuscles in millions, in 1 c.mm. of undiluted blood the total number

of corpuscles found in 80 squares of a 1 : 200 blood dilution be multiplied by 0.01. To determine the white corpuscles in thousands in 1 c.mm. of undiluted blood, one should multiply the total number of white blood-corpuscles found in 100 large squares by 0.025 if a 1 : 10 blood dilution be used. If the counting occupy a long time, or be done at high temperature, Bürker recommends that the preparation be protected against drying by means of a small moist chamber of tin, open on the top, and lined with moist blotting-paper.

THE HAYEM-NACHET HEMATIMETER

This very practical blood-counting apparatus depends upon the same principle as the older chambers, but differs from them in that the chamber of a given depth ($\frac{1}{5}$ mm.) is not ruled, and the cover-glass is not merely laid on, with the formation of Newton's rings, but is held down by the introduction of a drop of water, which spreads out by capillarity and fixes the cover-glass tightly.

In the older instruments, the counting was done by introducing into the ocular a counting-net similar to an ocular micrometer, the surface value of which must be estimated for the lens used and for the given tube length. Leitz also furnishes a similar apparatus. In the newer apparatus the ruling, or rather the counting-net, is projected from a small, transparent photographic positive, with a definite reduction in size, as a real picture on the floor of the chamber. This is accomplished by means of a small projection apparatus placed in the opening of the microscope stage. Both devices have the advantage that one can move the chamber as desired under the picture of the rulings, independently of the divisions, and always have a new part of the blood mixture under the counting-net. The photographic ruling is also superior, in that the deep black lines are more easily visible than the engraved lines of the Zeiss chamber. The network consists of 16 squares, which are arranged to form one large square, and it has vertical and horizontal lines in the small squares to facilitate orientation (Fig. 304). The counting can be best done by regulating the dilution, so that the large square may be used as a counting unit. (See below.) We then simply move the chamber until a sufficient number of such units has been counted. As to the number of squares that must be counted, the accuracy required has to be taken into account, as mentioned on pp. 756 and 758. (For calculation, see below.) By means of this apparatus the counting becomes particularly easy if one employ the counting microscope (microscope hématimétrique).[1] This is a small, inexpensive microscope, to the stage of which is attached a movable stage for the counting-chamber, in addition to the Hayem projection apparatus.

This stage is so constructed that it allows the counting-chamber to move crosswise exactly the distance of the diameter of a counting unit (a large square). The movement in the anteroposterior direction is accomplished by means of a small lever. We can thus count in the shortest possible time, and without any difficulty, the number of adjacent squares desired or even the entire preparation. The author recommends this counting apparatus on account of its deep black rulings and the simplicity and distinctness of the network, and the counting microscope is recommended on account of its convenient movable stage. The firm of Nachet provides, with this instrument, the convenient mixing apparatus described on p. 756 (mixing tray with ordinary pipet instead of mixing pipets).

When the Hayem-Nachet apparatus with projected counting-net is used, the calculation is done in the following manner: The counting mixture (for red blood-cells) is generally prepared by mixing $\frac{1}{2}$ cc. of the diluent, measured in the large pipet, with 2 c.mm. of blood, measured in the capillary pipet. Since, however, the larger pipet is not entirely emptied, and in the use of $\frac{1}{2}$ cc. of watery solutions 6 c.mm. remain within the pipet, an accurate dilution of 2 : 502 or 1 : 251 is not obtained, but rather a dilution of 2 : 496 or 1 : 248. The area of the larger square of the counting-net, which serves as the counting unit, is $\frac{1}{25}$ sq. mm., so that the cubic content of the counting unit, in a chamber with a depth of $\frac{1}{5}$ mm., is equal to $\frac{1}{125}$ c.mm. We, therefore, have to multiply the average number of the corpuscles per counting unit by 248 × 125 = 31,000, in order to obtain the number of red blood-corpuscles in 1 c.mm. of undiluted blood. If one proceed according to the directions on p. 756, *i. e.*, washing out the diluting pipet several times with the blood dilution, the correction for capillary adhesion is not necessary, and the dilution is 2 : 500 or 1 : 250 and the multiplication factor is 31,250. If we wish to have the same grade 757, it is acy as that obtained by the method with the Zeiss chamber, given on p. of accur- necessary, in order to use 1000 as the factor, to count 31 large squares and multiply by 1000.

[1] This can be obtained from the optical firm Nachet fils, Rue St. Séverin, Paris.

To count the leukocytes with the Hayem-Nachet apparatus (see p. 756) we mix 25 c.mm. of blood, diluted to the mark 500 on the large pipet (= 494 c.mm.) (see above), and then multiply the average leukocyte count for one counting unit (a large square) by 125 (as one counting unit has a capacity of $\frac{1}{125}$ c.mm.), and then by $\frac{519}{25}$ = 20.76, *i. e.*, a total of 2595. If we eliminate, as above described, the error due to capillary

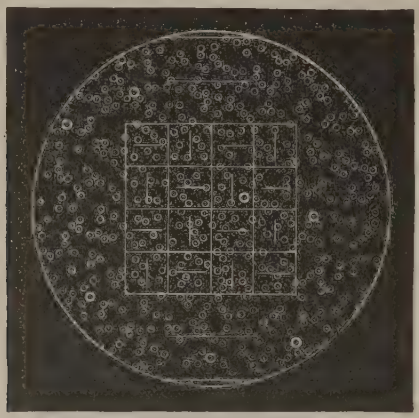


Fig. 304.—Field of the Hayem-Nachet counting microscope. The small squares have an area of $\frac{1}{400}$ sq. mm., the complete large square an area of $\frac{20}{400} = \frac{1}{20}$ sq. mm. The circle is the boundary of the field.

adhesion in the larger pipet, the multiplication factor is 2500. For complete accuracy at least 300 leukocytes should be counted. We, therefore, count through a number of units (large squares), calculate the average, and multiply by the given factor.

CORPUSCLE COUNTING AWAY FROM THE BEDSIDE

The methods for counting red and white corpuscles are such that they must be carried out directly, at the bedside or at least not far away. This is not difficult in hospital practice, but in private practice it is a very different matter, for the carrying of the microscope and all the necessities to the home of the patient is very inconvenient. The very easily transported counting microscope of Nachet is recommended for this purpose (p. 761). Since very few physicians possess this instrument, the author has experimented in order to find out if counting dilutions prepared at the bedside and sealed in glass capillary tubes could not be saved long enough to be taken from the bedside to the laboratory to be counted. He has found that this is possible for a short time only, because the corpuscles gradually clump in the mixture. He recommends that, when the counting cannot be done at the bedside, the undiluted blood be taken (with the addition of a substance to prevent coagulation) and the counting mixture be prepared at home. The best agent for preventing coagulation is hirudin, which also has a protective action on the leukocytes and blood platelets; or, since this is not always at hand, and is rather expensive, ammonium oxalate.

It is sufficient to put a few crystals of one of these substances on the wound, so that the blood comes immediately in contact with it. The blood is run into a capillary tube, and, where possible, the column of blood is placed in the middle and the ends of the tube are sealed off over an alcohol lamp. In order to prepare the counting mixture the ends of the tube are broken off and the blood is allowed to flow into a clean watch-glass. The dilution is then prepared in the ordinary way. Blood so kept (by the use of hirudin) can also be used for preparing smears. Very frequently the morphologic elements are too much changed for this purpose, and it is better to make the dry smear at the bedside, as it is not attended with any special difficulty.

NUMBER OF RED AND WHITE BLOOD-CORPUSCLES UNDER PHYSIOLOGIC CONDITIONS

The number of red blood-cells (Vierordt) in 1 c.mm. of blood is 5,000,000 in men and 4,500,000 in women. In Switzerland the counts show that healthy women have 5,000,000 or over, and men about 6,000,000. These correspond very well with the following figures, which Sörensen published to show the variation in the number of blood-corpuscles at different ages:

TABLE

	Males.			Females.		
	Age.	Number of red cells in 1 c.mm. of blood.	Number of individuals examined.	Age.	Number of red cells in 1 c.mm. of blood.	Number of individuals examined.
Newborn	5–8 days	5,769,500 (5,284,500–6,105,000)	3	1–14 days	5,560,800 (5,262,500–5,960,000)	6
Children	5 years	4,950,000 (4,750,000–5,145,000)	2	2–10 yrs.	5,120,000 (4,980,000–5,260,000)	2
Adults (Students)	19½–22 "	5,606,600 (5,422,000–5,784,000)	7	15–28 "	4,820,000 (4,417,000–5,350,000)	14
Adults (Young physicians)	25–30 "	5,340,000 (4,900,000–5,800,000)	6	41–61 " (Nurses)	5,010,000 (4,800,000–5,470,000)	7
Adults	50–52 "	5,137,000 (4,910,000–5,359,000)	2			
Adults	82 "	4,274,000	1			

In an examination carried out by Frl. A. Perlin, under the direction of Stooss,[1] the normal number of red blood-corpuscles in childhood are given as follows:

Age.	Number of cases examined.	Red blood-corpuscles. Minimum.	Maximum.
2 to 18 months	17	4,200,000	5,400,000
2 years	13	4,750,000	5,600,000
3 "	7	4,800,000	5,350,000
4 "	13	4,000,000	5,500,000
5 "	16	4,700,000	5,600,000
6 to 9 years	7	4,200,000	6,000,000
11 to 14 and 16 years	7	4,800,000	6,000,000

From both of these tables, Sörensen's as well as Perlin's, we find that the number of red blood-corpuscles in healthy individuals have at least the same, if not a greater, variation than the hemoglobin content. For this reason, the estimation of the so-called hemoglobin quotient (p. 765 et seq.) and volume quotient (see p. 785 et seq.) is attended with certain inaccuracies.

A number of physiologic conditions have some influence upon the number of red blood-cells. As to the influence of food, authorities differ. According to the observations of Vierordt and Limbeck, there is usually a slight diminution in the number of red cells after eating or drinking, probably to be explained by the dilution of the blood due to absorption of fluid. On the other hand, fasting produces a relative increase. Obese people average a somewhat lower red blood-cell count than thin people (Leichtenstern). Menstruation and pregnancy seem to have no especial influence upon the number of blood-cells. Cathartics and diuretics increase the number of red cells if their action be very marked, possibly on account of the removal of water. A cold bath temporarily increases the number of red cells. This depends merely on the changes in distribution of the cells on account of changes in the

[1] Jahrbuch für Kinderheilkunde, N. F., vol. lviii.

circulation. The influence of climates and high altitudes upon the number of red blood-corpuscles is interesting. According to Viault, Miescher, Egger, Jaquet, and others, the number of red blood-cells is considerably increased in altitudes of 1000 to 2000 meters above the level of the sea. This increase occurs within a very short space of time. In Arosa, Egger found that inside of two weeks the number of red blood-corpuscles increased in newcomers from 5,000,000 to 6,000,000. Egger has proved that this increase is due neither to diminution of the plasma, owing to the dry air of the high altitude, nor to a mere difference in the distribution. (See Miescher's works on histochemistry and histology, Leipzig, 1897.) Gottstein claimed that this state of affairs was an illusion, due to the fact that the depth of the counting-chamber was greater with a low than with a high air-pressure; but physics contradicts such an hypothesis. Besides, the hemoglobin percentage increases correspondingly.

In estimating the number of erythrocytes or leukocytes in any given case we must consider that the results are greatly influenced by the condition of the blood-current, the corpuscular elements being increased in the slow capillary current from which counting samples are taken, for, where the blood flows slowly, they are, for physical reasons, more numerous than where it flows swiftly. There is also a normal difference in the number of cells in the blood from different parts of the body; and in stasis the variations in the speed of the current are even greater than when the circulation is normal. The relations mentioned hold good only in stationary conditions, since then the cells are washed away through the finger-prick, because of the decreased resistance and the acceleration of the current following the wounding of the skin. If, on the contrary, the examination be undertaken at a moment when a change of circulation occurs in the pricked area, the results may be just the reverse, since in slowed currents the plasma comes out in advance of the corpuscles, and the less rapid circulation gives a blood richer in plasma and poorer in corpuscles, while the rapid circulation gives a blood richer in cellular elements.

Now, since the blood does not flow at the same rate through all parts of the body, even under physiologic conditions, conclusions as to the total cellular content of the blood, based on the results of counting, can only be drawn with the greatest precautions. Many changes in circulation, induced by hydrotherapeutic measures, the influence of light, etc., which have hitherto been considered without any question as the expression of a general variation of the red or white blood-corpuscle content, are really only the results of local changes in quantity and rapidity of the current of blood in a given part of the body, because of which, as in the punctured finger, sometimes more, sometimes fewer, corpuscles are obtained. These same factors may even give rise to error in interpreting the leukocytosis of infectious diseases, and are also of importance in the viscosity tests of the blood (see p. 850), in so far as the latter are not concerned with isolated plasma, but with the total blood, since the corpuscular content of the blood determines the degree of viscosity.

Rieder (*loc. cit.*) examined fasting people, and found that the ratio of the white to the red blood-cells in healthy adults with a normal red blood-count is 1 : 651, and in children (nine to fifteen years) 1 : 518. Considering the varying number of red cells, these comparative figures are of less value than the absolute number per cubic millimeter. Reider found in fasting adults an average number of 7680, and in children 9660. (See p. 797 with reference to the increased number of leukocytes in the newborn.)

Miss Perlin (*loc. cit.*, see above) gives the following as normal leukocyte counts for children:

Age.	Leukocytes. Minimum.	Maximum.
2 to 18 months	8800	15,000
2 years	8240	13,400
3 "	8900	11,600
4 "	8600	13,400
5 "	8800	11,200
6 to 10 years	7800	9,220
11 to 14 and 16 years	7000	8,900

NUMBER OF RED BLOOD-CELLS AND PERCENTAGE OF HEMOGLOBIN IN BLOOD UNDER PATHOLOGIC CONDITIONS; THE HEMOGLOBIN QUOTIENT OF THE RED BLOOD-CELLS

(See also the blood-findings in the individual blood diseases, p. 823 et seq.)

All conditions included under the title "anemia" produce a more or less marked diminution in the number of red blood-cells and in the hemoglobin. Any acute or chronic illness may diminish both the number of blood-cells and the amount of hemoglobin, and so produce an anemia. This is, however, by no means always the case. In acute febrile infectious diseases the red blood-corpuscles and the hemoglobin are as often increased as diminished, the increase being due to the diminution in the amount of blood-plasma, the decrease to the retention of the water and the destruction of the red blood-cells. (See p. 798, The Blood in Infectious Diseases.)

Chronic cachexia generally tends to diminish both the amount of hemoglobin and the number of red cells. In the cachexia of cancer the anemia may be very marked and of diagnostic importance. Whenever a marked anemia accompanies cancer, the growth has almost always caused a loss of blood. This loss may be very gradual and not noticed at the time (carcinoma of the stomach and intestines). A gastric cancer, through its profound disturbance of gastric chemistry (achylia) may give rise to pernicious anemia. (See p. 827 et seq.) The blood of tuberculous patients shows at times a diminished quantity of hemoglobin and a smaller number of red blood-corpuscles. This is, however, by no means the rule. Many tuberculous patients with marked pallor and cachexia frequently show a normal blood. Neurasthenic patients rarely show a diminution in the coloring-matter of the blood. Determining the amount of hemoglobin in these cases is of great value with reference to the treatment, as the author has repeatedly emphasized, for a pale appearance is often deceptive. (See section on the Color of the Skin, p. 38 et seq., and p. 823, Blood-findings in the Individual Anemias.)

In venous congestion both the hemoglobin and the number of blood-cells are increased. This is a purely mechanical result, due to the slowing of the blood-stream, which leaves the blood-cells in the capillaries. (See p. 763.) This finding does not exclude an increase in the amount of water contained in the blood-plasma, nor hydremic plethora.[1]

The Hemoglobin Quotient or Hemoglobin Value of the Red Blood-corpuscles (*Color Index*).—If the quantity of hemoglobin and the number of blood-cells in any given disease be expressed in percentages of the normal, and the percentage of hemoglobin be divided by the percentage of the number of red cells, a fraction is obtained which, as will readily be seen, indicates how much hemoglobin any one blood-cell contains, as compared with the normal amount. This fraction is called the color index, the blood-corpuscle quotient or value. In order to avoid confusion with the volume quotient described on p. 785 et seq., the author would suggest using "hemoglobin quotient" or "hemoglobin value." Normally this equals 1, but in certain anemias it is sometimes more (pernicious anemia), sometimes less (chlorosis) than 1.

Unfortunately, there exists a good deal of uncertainty in the estimation of the hemoglobin quotient, on account of the fact that the hemoglobin content, as well as the number of red blood-corpuscles, may vary considerably. An exact calculation of the quotient would, naturally, be possible only if there were a fixed normal for

[1] See K. Baranoff, Beiträge zur Theorie der Flüssigkeitsentziehung und der Behandlung der Circulationsstörungen, I. A. D., Bern, 1895.

the content of hemoglobin, as well as for the number of red blood-corpuscles. Such a normal must, therefore, be supposed, but then the quotient has but a limited value, as the variations from the normal are not large. There remains no other alternative than to use either the corrected hemoglobin percentage for such estimations (see p. 753), or to use the average of the physiologic extremes as the normal. The hemoglobin content, using the author's hemometer with the new standard solution, is $\frac{80 + 100}{2} = 90$ for men, and $\frac{70 + 90}{2} = 80$ for women.

The number of red blood-corpuscles in an adult, according to Sörensen (p. 763), is 5,000,000. We then have to express the values found as fractions of these normal points in order to find the quotient. If, by the author's new hemometer one obtain a reading of 70 with 4,000,000 red blood-corpuscles, the calculation of the quotient should be done as follows, considering 5,000,000 as the normal number of red corpuscles.

The hemoglobin quotient:

$$Q = \frac{\frac{70}{90}}{\frac{4}{5}} = \frac{350}{360} = \text{about } 1.$$

ESTIMATION OF THE CORPUSCULAR VOLUME; SEDIMENTATION OF THE BLOOD, AND HEMATOCRIT EXAMINATIONS

The relation of the corpuscular volume to the total volume of the blood in a given unit was previously estimated by allowing the blood to sediment in a graduated glass tube after the addition of a substance retarding coagulation, such as sodium or ammonium oxalate or hirudin. The height of the layer of corpuscles in proportion to the height of the total quantity of blood was then read off. This method, however, has not been adopted, for in human blood, as opposed to horse's blood, where this method is very useful, the corpuscles settle so slowly that, in the interval, chemical changes occur which materially influence the result. Hedin[1] recommended that sedimentation be hastened by centrifuging, and in order to use the smallest quantity of blood possible, he employed the so-called hematocrit, a graduated thermometer tube open at both ends and closed during the act of centrifuging by means of rubber caps. This method has been adopted and modified by Eykmann,[2] Hamburger,[3] Gärtner,[4] and Köppe.[5] The centrifuging must naturally be continued until the column of cells remains a constant height.

Originally, the blood for the hematocrit examination was mixed with special chemicals to hinder coagulation, such as Müller's fluid or ammonium oxalate. Since, however, these solutions are neither chemically nor physically inactive, and since, if they be not made isotonic with the blood, they artificially change the corpuscular volume, control experiments must be done in each case in order to prepare a solution that is isotonic with the blood. When oxalates are employed, a precipitate of calcium oxalate is deposited with the corpuscles and so alters the volume. For these reasons it is properly recommended by more recent writers that such substances delaying coagulation be not used, and that coagulation be hindered by various other means.

Köppe (*loc. cit.*) coated the inner surface of the hematocrit tube with a thin layer of cedar oil, which, as is well known, retards coagulation. Just enough of this is drawn up in the tube to moisten the entire inner surface. The blood to be tested is placed immediately in the capillary tube, which is then sealed and centrifuged. The reading of the height of the column of blood before centrifuging will give erroneous results, since noticeable quantities of oil would then be reckoned as blood. After the centrifuging the oil, by virtue of its lightness, appears on top of the column of blood, so that a reading taken at this time will give accurately the height of the column of blood (or, rather, corpuscles and plasma reckoned together), sharply marked off from the oil, and also the height of the corpuscular layer. Since the slightest impurity of the oil or irregularity of the wall of the tube may produce coagulation, Köppe recommends that several tubes be centrifuged together or consecutively, and that sharply defined columns and harmonious results from the various tubes should be demanded.

[1] Skand. Arch. f. Physiol., 1892; and Pflüger's Arch., 1895, vol. lx.
[2] Pflüger's Arch., 1895, vol. lx.
[3] Osmotischer Druck und Ionenlehre, 1902, pp. 514 and 379.
[4] Allgem. Wiener med. Zeitung, 1892.
[5] Arch. f. (Anat. und) Physiol., 1895.

Hamburger, in order to prevent interference by coagulation, used defibrinated blood. He prepares a small glass tube, with a capacity of about 0.5 to 1 cc., sealed at one end, corked at the other. He places a few glass beads in the tube, fills it with the blood to be examined, closes the tube, and shakes for fifteen minutes in order to defibrinate. The blood is then filtered through a very small filter, in order to free it of the particles of fibrin, and 0.06 cc. of the filtrate is then measured by means of a capillary pipet, placed in one of the hematocrit tubes to be described later, and centrifuged until a constant corpuscular volume is obtained. After shaking the blood with glass beads the serum is stained somewhat red, but, according to Hamburger, this does not give rise to any error in the reading of the corpuscular column, because only a very few corpuscles contribute to this staining. Hamburger employs, instead of the ordinary hematocrit tubes, which are open at both ends and have to be closed by a special device, a graduated tube of the form and size shown in Fig. 305, sealed at one end and funnel shaped at the other. These same tubes are used for determining the osmotic pressure described on p. 768.[1] The blood should be made to flow slowly from the pipet into the funnel-shaped end of the tube. No noticeable amount of blood is left in the pipet. Hamburger oils the point of the pipet to prevent the last drop of blood from adhering to it. The author recommends the Hamburger tube, as he has had some very unpleasant experiences with the original hematocrit tubes, because they leak very readily. The tube is easily cleaned by filling the funnel-shaped part with water, and dislodging the sediment which lies in the capillary portion of the tube with a thin strip of whalebone. The mixture is shaken up and poured out several times until the tube is apparently clean; the remainder of the organic substances is totally removed by rinsing with a mixture of sulphuric acid and potassium dichromate. It is again rinsed thoroughly with distilled water and dried with alcohol and ether.

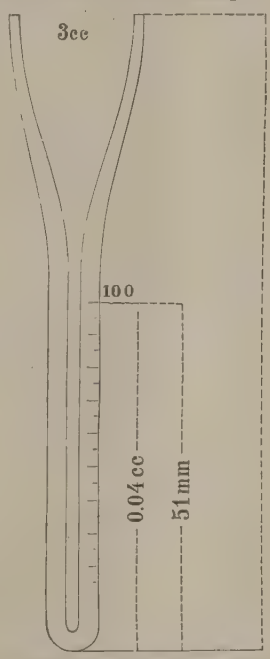


Fig. 305.—Hamburger's hematocrit tube. Actual size.

Kottmann prevents coagulation by the addition of dry hirudin. In his method of estimating the blood-mass (see p. 732) he allows the blood to flow directly from a vein into a glass containing a weighed or an estimated amount of hirudin. If we wish to carry out this method on the capillary blood obtained from the finger in the ordinary way, the hirudin powder is dusted on the finger immediately after making the puncture, so that the blood mixes with it as soon as it appears on the surface. Since hirudin is very soluble, practically hygroscopic, a sufficient mixing is spontaneously and immediately obtained. The mixing can be made more complete later on by drawing the blood in and out of the capillary pipet. The action of good (fresh) hirudin in preventing coagulation is so marked (1 mg. prevents the coagulation of .5 cc. of blood) that a hardly measurable quantity is necessary for hematocritic experimentation. The volume of blood, therefore, and its osmotic concentration, is not influenced to any noticeable extent by the hirudin added.

Finally, Capps[2] employs the hematocrit for estimating the volume quotient of the blood (see p. 785) by centrifuging the blood without adding anything, and disposes of coagulation by using a very powerful and rapid electric centrifuge, which sediments the corpuscles completely before coagulation begins. This procedure meets with difficulties in case the coagulability of the blood be very markedly increased.

The objection that a change in the volume of the blood-corpuscles is induced by the addition of non-isotonic solutions must now be discredited, on account of improved technic, but there is still the objection that a certain amount of fluid remains mixed with the corpuscles and is measured along with the corpuscular volume.

[1] In this connection see p. 769, note 2.
[2] Amer. Jour. Med. Research, 1903, vol. x, No. 3.

Eykmann has found (Pflüger's Arch., 1895, vol. lx, p. 340) that this error may be eliminated by using a rapid centrifuge (2600 revolutions a minute) for one and one-half hours. The corpuscular volume found must then be multiplied by 0.9025. Centrifuging for so long a time is, however, hardly necessary for practical purposes, and it has been ascertained that useful relative values are obtained by centrifuging for such a time that there is no noticeable change in the corpuscular volume reading after centrifuging an additional two minutes. To obtain this result quickly the weight of the centrifuged mass must be as light as possible. This is obtained by procuring with the centrifuge some lightly made hematocrit arms, which may be easily inserted in place of the ordinary heavy ones. These should be so delicately made that they offer but slight resistance to the air. In using the Hamburger tubes it is necessary, for mechanical reasons, to fasten the tube directly in the ring by a cork. In the ordinary clinical centrifuge these rings support the aluminum cups which hold the glass centrifuging tubes. When these cups are removed, the weight of the moving mass and the atmospheric resistance is so markedly reduced that, even without special hematocrit arms, a decided increase in the number of revolutions is obtained.

The author believes that if the improved technic be employed, and the precautions above described be carefully regarded, the hematocrit examination should again be made use of clinically. It was mainly discredited on account of faulty methods, and also by the fact that observers expected to see, contrary to fact, a definite relation between the number of corpuscles and their volume. This is naturally impossible on account of the very unequal size of pathologic corpuscles. In spite of this we should observe that a comparison of the counting results with the findings by the hematocrit examination gives valuable information, because it allows an estimation of the so-called volume quotient, *i. e.*, the average volume of an individual corpuscle, and also because the percentage volume of the corpuscles in the blood may be of clinical interest, particularly in following up the changes of the osmotic condition of the blood at short intervals of time. For criticism on the hematocrit methods the reader is referred to Hedin, Eykmann, and Köppe (*loc. cit.*). The red blood-corpuscles in normal cases form about one-half the volume of the blood. Ordinarily, this corpuscular volume is expressed as percentage of the blood-mass, so that the normal red corpuscle volume is about 50 per cent. The method of calculation with the Hamburger tube is shown in Fig. 305.

In centrifuging out the corpuscles a thin, whitish layer may be recognized on top of the layer of red cells. This is composed of white corpuscles, and at times a similar layer of a somewhat different shade, due to blood-plates. Marked grades of leukocytosis, as in leukemias, may be recognized in this way without further examination.

POWER OF RESISTANCE OF THE ERYTHROCYTES TO HYPOSMOTIC AND OTHER INJURY

It is well known that when a small amount of blood is placed in an excessive quantity of a hypotonic saline solution, the blood-pigment passes out of the erythrocytes, so that a so-called laked blood results. In such experiments the stromata of the erythrocytes are not dissolved. In saline solutions which are isotonic or hypertonic to the blood-plasma, the blood-pigment does not pass out, at least not within a limited period of time. For this reason it was formerly believed that the osmotic pressure of the blood-plasma could be determined by finding the concentration of the saline solution which would preserve the erythrocytes intact. It has nevertheless been shown that the escape of the hemoglobin from the erythrocytes under these conditions is by no means a purely osmotic phenomenon, but that it is also dependent upon the specific sensibility of the stroma of the erythrocyte, which holds the hemoglobin within the corpuscle. This has been absolutely proved by the observation that all of the erythrocytes of an individual are not equally sensitive to the same hypotonic solution. In a slightly hypotonic saline solution the osmotic concentration of which closely approximates that of the blood, a number of erythrocytes are destroyed by the escape of their hemoglobin, while others do not lose their pigment until the saline solution is much more markedly diluted. This could not be the case were the phenomenon purely osmotic in character. For this reason we are no longer justified in assuming that the osmotic concentration of the blood-plasma may be indirectly obtained by determining the resistance of the erythrocytes to saline solutions of varying concentration. This false idea is also responsible for the incorrect supposition that a saline solution of 0.7 or even 0.6 per cent. is physiologic, *i. e.*, isotonic with the blood-plasma, when, as a matter of fact, the direct determina-

tion of the osmotic pressure of the blood by means of cryoscopy (see p. 845) has shown that a 0.9 per cent. saline solution is isotonic with human blood.

Hamburger[1] proposed a method for estimating the resistance of the red corpuscles to hypotonic salt solutions, using for these determinations a large number of funnel-shaped tubes.[2] (See p. 767.)

The tubes are prepared with 2 cc. of saline solution of different strengths, each one varying from the next by about 0.01 per cent. To each tube 0.05 cc. of blood is added, by means of a capillary pipet, and the mixture is stirred up with a strip of whalebone. This latter procedure also removes the air from the capillary part of the tube. After standing for fifteen minutes the tubes are centrifuged, and one then notes by contrasting the fluids that have become clear, the concentration in which there is the faintest trace of hemoglobin stain in the salt solution, and the concentration in which the maximum hemolysis, *i. e.*, the complete surrendering of the coloring-matter, is reached. The solution with which we obtain the minimum hemolysis shows the minimum resistance, while that giving total hemolysis represents the maximum resistance, and the solutions between these extremes represent the range of the resistance. The fact that the surrendering of the coloring-matter by the corpuscles is not always complete in a given dilution is explained, according to Hamburger, by the supposition that individual corpuscles have different resistances. Hamburger emphasizes the fact that the results of the examination of the blood for resistance to varying osmotic pressures are hardly comparable unless carried out with the technic proposed by him and with the employment of his tubes. On account of the influence of the oxygen, or rather carbonic-acid content of the blood, on the resistance of red blood-corpuscles as shown by Hamburger, it is recommended that the blood be spread out on the funnel-shaped portion of the tube in contact with the air for several seconds before mixing it with the salt solution, so that the corpuscles may first take up the oxygen of the air.

According to Hamburger's investigations, the resistance of the red blood-corpuscles to osmotic destruction is a very complex phenomenon, from which no definite clinical conclusions can as yet be drawn, since we do not know the determining factor in any given case. Hamburger states rightly that a decreased resisting power found by his method in no way shows, of itself, a diminished resistance of the stroma of the corpuscles against osmotic swelling, since, according to his theory of the structure of the stroma (reticular structure), besides the resistance of the network, the swelling capacity of the blood-corpuscle content, or its osmotic pressure, as well as the percentage volume of the swollen content in proportion to the stroma, are additional factors. Unfortunately, it is not decided which factors determine the result, as only one, namely, the swelling power which corresponds to the osmotic pressure of the blood, can be directly estimated.

P. Ribierre's[3] method is similar to the above. This writer uses a 0.5 per cent. salt solution, and places in a very small test-tube 50 drops; in a second, 48; in a third, 46 drops, etc., and then adds distilled water sufficient to make 50 drops in each tube. A definite amount of blood (20 c.mm.) is put into each tube from the capillary measuring pipet (p. 744). Normally, the hemolysis begins in a tube containing 44 drops of salt solution and 6 drops of distilled water, and is complete in the fifth or sixth following tube. The results are described as "slight," "distinct," "very distinct," and "complete," and one states in which of the dilutions these grades of hemolysis are found. French writers previously represented the results of these determinations in the form of a curve, the abscissa of which represented the number of drops of salt solution used, and the ordinates represented the four grades of hemolysis.

One can then easily calculate at what percentage concentration the hemolysis begins. If, for instance, the tube containing 44 drops express the extreme concentration, the percentage will be $\frac{44}{50} \cdot 0.5$ per cent. = 0.44 per cent.

With a sensitive blood, Ribierre begins with stronger saline solutions, *e. g.*, 0.7 per cent., and puts in the first tube 70 drops; in the second, 68; then, 66, 64, etc., and adds distilled water up to 70 drops in each case. If hemolysis begin in the tube containing 64 drops, the saline concentration is $\frac{64}{70} \cdot 0.7$ per cent. = 0.64 per cent.

According to Hamburger,[4] marked decrease in the resistance of the red blood-

[1] Arch. der Physiologie, von Du Bois Réymond, 1886, p. 476; 1887, p. 31. Zeit. f. Biol., 26, new series, viii, p. 414. Also Hamburger, Osmotischer Druck- und Ionenlehre, Wiesbaden, 1902.

[2] These may be obtained from the glass-blowing works in Amsterdam, Sprint straat, 303.

[3] Thèse de Paris, 1903.

[4] Osmotischer Druck- und Ionenlehre, Wiesbaden, 1902, p. 365.

corpuscles to injury by hyposmotic solutions has been found in fever, chlorosis, pernicious anemia, and cyanosis. Strong resistance of the red cells to hyposmotic solutions has been found in carcinoma and jaundice. Clinically important results have been found in jaundice by Chauffard,[1] who found, by Ribierre's method, that obstructive jaundice can be differentiated from other types, designated by the writer as "hemolytic" (terms which correspond with "hematogenous" or "hematohepatogenous" jaundice, see p. 44 et seq.), by the fact that in obstructive jaundice the resistance of the red blood-cells to hyposmotic destruction is raised, while in hemolytic jaundice, on the contrary, it is lowered. We may, therefore, using Ribierre's method, find in obstructive jaundice hemolysis beginning in a concentration of 0.36 to 0.38 per cent., *i. e.*, in a tube made up of 36 or 38 drops of a 0.5 per cent. salt solution, with the addition of 12 and 14 drops of distilled water. In hemolytic jaundice, on the other hand, hemolysis begins at 0.4 per cent. Chauffard found a lessened resistance especially in pernicious anemia with jaundice, and in the so-called "hereditary jaundice" of Minkowski. This agrees exactly with Minkowski's explanation, which is that this is a hematogenous, or rather hematohepatogenous, jaundice, due to destruction of red blood-cells which appears in the disease which accompanies splenomegaly, as a result of splenic changes.

The determination of the power of resistance of the erythrocytes to hyposmotic injury is not sufficient to settle all the questions in reference to their resisting power, since Chvostek [2] (in contrast to Murri), found that in paroxysmal hemoglobinuria the power of resistance of the erythrocytes to saline solutions is normal, while they show but slight resistance to mechanical injury (shaking) and to stasis within the body.

The peculiar behavior of red blood-cells in this disease under the influence of cold is mentioned on p. 44.

The testing of the resistance of red blood-corpuscles to specific hemolytic action, for example, the saponins, is worthy of clinical investigation.

OTHER MORPHOLOGIC RELATIONS OF THE BLOOD

TECHNIC OF THE MICROSCOPIC EXAMINATION OF THE BLOOD

For this purpose either fresh or stained dried preparations may be employed.

MICROSCOPIC EXAMINATION OF FRESH BLOOD

The most important alterations in the blood which are peculiar to diseases of the blood proper may be recognized in fresh specimens. Certain precautions should be taken in preparing the latter. Too much pressure applied near the puncture to increase the flow may deform the red blood-corpuscles. If, however, the blood will not flow without it, light pressure may be applied at a little distance from the puncture. A scrupulously clean cover-slip should be very gently touched to the drop of blood, so that only a very tiny amount of blood adheres. Too large a drop makes too thick a preparation and too pronounced a rouleaux formation, so that the finer details cannot be detected. The cover-slip is immediately dropped very carefully upon a clean slide. Delay will allow drying and consequent deformity of the cells. Pressure on, pulling, or sliding the cover-slip should be avoided. Unless these precautions are observed, a most beautiful microcytosis or poikilocytosis (see below) may be artificially produced. The blood should be distributed under the cover-slip in a uniformly thin layer, but this effect must be produced entirely by capillary action. The preparation should be examined immediately, because the blood-corpuscles soon begin to shrink from loss of water, and to assume all

[1] Semaine Med., 1907, No. 3.
[2] Ueber das Wesen der paroxysmalen Hämoglobinurie, Wien, F. Deuticke, 1894.

sorts of bizarre shapes. Such a preparation can be preserved for a limited time if evaporation be prevented by smearing the edge of the cover-slip with oil. Diluting fluids should be avoided.

The variation in size and shape of the red blood-corpuscles (poikilocytosis (see p. 782 et seq. and p. 785 et seq) can easily be recognized in unstained preparations if the smear be sufficiently thin. The color variations (variations of hemoglobin content, anisochromia) of the red blood-corpuscles can also be seen. This generally goes hand in hand with the variations in size and shape, and, like these, is seen best in severe pernicious anemia. (See pp. 783 and 826.) The basophilic granules of the red cells (see p. 784) can occasionally be recognized in a fresh smear as colorless spots. An experienced observer can recognize also the nucleated red cells (see p. 784 et seq.) in fresh smears, and may even be able to differentiate normoblasts from megaloblasts by the size of the nucleus and the rim of protoplasm. The red-cell nucleus appears in these fresh smears as a sharply defined, colorless area inside of the red blood-corpuscles. The inexperienced observer must be careful not to mistake a well-marked and peculiarly light central depression in the corpuscle for the nucleus. In all doubtful cases, of course, the smear must be stained and examined.

Examination of the Blood in Reference to the Formation of Rouleaux

Under normal conditions, in fresh microscopic blood-specimens which are not too thin, we find the red blood-corpuscles, as a result of their peculiar disk-like shape and the viscosity of the blood, standing upon their edges and arranged in cylindric conglomerations which have been compared to a roll of coins. This formation occurs in the circulation only when the blood stagnates, but it normally occurs quite rapidly (in a few seconds) outside of the body. This process is known as the formation of rouleaux. It is evident that the formation of rouleaux must be influenced by the number of the red blood-corpuscles. We consequently find a diminished formation of rouleaux in all conditions which are associated with a diminution in the number of the red blood-corpuscles, and with a properly made specimen the diminished tendency to form rouleaux may be made the basis of a probable diagnosis of a decreased number of red blood-cells. By a properly prepared specimen is meant one having a sufficient thickness to allow the erythrocytes to stand upon their edges. If the preparation be too thin, the erythrocytes are flattened out by the cover-glass and cannot adhere to each other by their flat surfaces. When a specimen of proper thickness is immediately examined, individual erythrocytes should be visible standing upon their edges. In order to obtain a layer of blood of the requisite depth, we should vary the size of the drop of blood upon the slide and avoid exerting any pressure upon the cover-glass. The specimen should not be too thick, since this interferes not only with the formation of rouleaux, but also with their recognition. Poikilocytosis, as well as a diminished number of erythrocytes, naturally tends to prevent the formation of rouleaux. From our investigations thus far we cannot say whether the formation of rouleaux is disturbed by a diminished viscosity of the blood.

Microscopic Determination of the Amount of Fibrin in the Blood

In addition to the quantitative estimation of the separated and purified fibrin from a given quantity of blood,[1] the microscopic examination of a fresh blood-specimen may sometimes give a fair idea of the amount of contained fibrin. If a fresh blood-specimen be protected against drying by smearing the edges of the cover-glass with paraffin, and be allowed to stand for a quarter or a half-hour, the separated fibrin may be recognized by strong magnification in the shape of a fine network more or less distinctly spread out between the red blood-corpuscles. In order to form a conception of the quantity of fibrin present, the thickness of the specimen must be

[1] After washing the clot with chloroform water, alcohol, and ether, the quantitative estimation may be made either by weighing or by Kjeldahl's method.

considered, since, other things being equal, the thicker the specimen, the more marked will be the fibrin network. If the specimen be very thin, the fibrin network may entirely escape observation. A place in the specimen should consequently be selected which fulfils the requirements laid down for the examination of the blood for rouleaux (see above), *i. e.*, immediate observation should reveal isolated red blood-cells standing upon their edges, and, subsequently, distinct spaces should be seen between well-formed rouleaux. When the blood is rich in fibrin, as in inflammatory affections and particularly in pneumonia, the spaces between the rouleaux are entirely filled by a thick fibrin network; while if the blood contain but little fibrin, it is concentrated about the collections of blood-platelets, in the shape of poorly formed stars. In general the quantity of fibrin in the blood goes hand in hand with the degree of leukocytosis; and in leukopenic diseases, such as typhoid fever, a pronounced diminution of the amount of fibrin is consequently not without diagnostic importance.

PREPARATION AND STAINING OF DRIED SPECIMENS

The staining of the histologic elements of the blood is almost exclusively confined to dry preparations. These stained specimens give information in regard to the granulation of the leukocyte protoplasm discovered by Ehrlich, as well as to the coarser morphologic conditions and staining properties of the nuclei and of the protoplasm of all the blood-cells. Ehrlich, by a careful study of the staining peculiarities of the granulations with various anilin colors, has found that with given mixtures of anilin dyes they possess elective affinities and stain differently. He classifies the available anilin dyes, which are chemical salts, into an *acid group*, in which the acid radicle, and a *basic group*, in which the basic radicle, determines the staining property of the dye, and further into a *neutral group*, in which both radicles possess staining properties. *Eosin* and *acid fuchsin* are types of acid stains, *methylene-blue and methylene-green* of basic stains, and *rosanilin* and *picric acid* of neutral stains.

He found that certain granulations in the white blood-corpuscles stained only with acid, others only with basic, stains; a third group could be stained with both dyes, and a fourth by neutral pigments only. On the strength of this he distinguishes (α) oxyphilic or eosinophilic, (β) amphophilic, (γ and δ) basophilic, (ε) neutrophilic granulations. The difference between γ and δ is chiefly in the size of the granules. The (γ) granules are the so-called *mast-cell granules;* they are basophilic and larger than all the others. According to Ehrlich, each leukocyte normally contains only one kind of granule. Exceptions to this rule occur in pathologic cases. (See p. 836.) The β and δ varieties are not found in human blood.

Preparation of the Dry Blood-smear

The blood must first be spread in a thin, uniform layer on a glass slide and allowed to dry. Formerly cover-glasses exclusively were used for this purpose, but more recently slides have been employed with considerable advantage, on account of their larger size. Very thin cover-slips (less than 0.1 mm.) should be cleansed with the utmost care. Fat can be removed with a mixture of ether and alcohol and a soft linen cloth without shreds.[1] The cover-glass must be of room temperature when used, for if too cold, vapor will condense on it and easily spoil the smear. For handling the cover-glass Ehrlich's "forceps"

[[1] Soap and hot water and careful rubbing with a soft linen cloth will cleanse them thoroughly. Occasionally it may be necessary to wash new cover-slips in strong acid to remove the glaze.—Ed.]

(a clasp with broad, almost knife-like edge) is recommended. By means of this a cover-glass can be readily picked up from a perfectly flat surface. A number of cover-glasses, sufficient for several blood examinations, are usually prepared beforehand, and are placed in the ordinary dust-free cover-glass case, in which they are easily carried about. In subsequent manipulations the cover-slips should be touched only with dry finger-tips or with forceps, and best at the corner. A very minute drop of fresh blood from the tip of a finger or the lobe of the ear is touched to a cover-slip, and a second cover-slip laid on top of this without pressure. Within a few moments, by capillary action, the blood will spread out between the cover-slips in a uniform layer; then, without exerting any pressure, the slips can be *slid* rapidly apart and dried in the air. Care should be taken not to breathe upon the cover-slip, otherwise the preparation may be spoiled.

To prepare a dry smear on a slide we must have the same regard for absolute cleanliness. For smearing the blood, a carefully cleaned cover-glass is used, and in order to obtain an even smear, it is best to use the ground cover-glass supplied with the counting chamber. (See p. 755.) The method of procedure is as follows: Place in the middle of one edge of a cover-glass a very small drop of fresh blood, not much larger than the head of a pin, holding the cover-glass meanwhile by the opposite edge. The edge of the cover-glass holding the drop is brought into

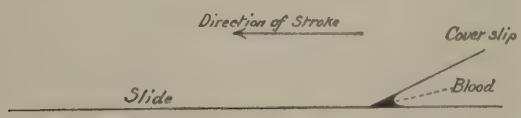


Fig. 306.—Preparation of dried smears on slides.

contact at an acute angle (as shown in Fig. 306), with the upper surface of the slide as it lies flat on a table. The blood spreads by capillarity along the entire edge of the cover-glass in the acute angle between it and the slide. The cover-glass should now be moved with moderate speed in the direction of the arrow in Fig. 306, *i. e.*, away from the acute angle along the surface of the slide.[1] In this way an almost instantly dried thin blood-smear is obtained, which is preferable to the cover-glass smears, both on account of the large surface as well as the uniformity of the layer. This uniformity of the smear, as well as the possibility, in a differential leukocyte count, of being able to count in one smear a large number of leukocytes on account of the large area, in the author's opinion assures for the future the slide method of obtaining smears. Besides this, the preparations on slides have the advantage that they can be more easily carried and are much less breakable. The clean slides, or those already used for smears, are carried in a dust-proof case with separate divisions. Such cases are easily obtained from any dealer in microscopic supplies. The method of staining slide preparations is practically the same as that for the cover-glass specimens. The author describes in the following paragraphs any special procedures employed.

[1] If one smear the blood in a direction opposite to that indicated by the arrow, the corpuscles are injured as a result of the pressure by the cover-glass.

Fixation of Dried Smears

Fixing or hardening of the dry preparation can be accomplished by drying in the air, or, according to Ehrlich's original method, by heating in an incubator at 110° to 120° C. for several minutes up to several hours, according to the stain used.

The Victor Meyer toluol oven is especially well adapted for this. It consists of a double-walled copper chamber, the jacket of which is three-quarters filled with toluol. The toluol is brought to boiling, and the apparatus is so arranged that the toluol vapor is condensed by being cooled with flowing water. The temperature of the inner chamber is that of the boiling-point of toluol (111° C. with normal barometric pressure), and it cannot be exceeded. We must carefully watch the cooling of the vapor in order to avoid fire. To obtain a gradual heating by this method it is advisable not to place the cover-glass directly upon the metallic portion of the inner chamber, for it will then immediately take on the temperature of the oven; it should be placed in the oven on a slide at room temperature, in which case the heating will be more gradual and more general. In employing slide smears this occurs without any special precautions, for here the preparation can only take up the temperature of the oven gradually. The heating can be kept up, according to the method of staining employed, from one minute to one or more hours. If a higher temperature than that obtainable by toluol (111° C.) be required for fixation, the oven may be filled with xylol (boiling-point, 139° C.), or with oil of turpentine (boiling-point, 150° C.), or with a glycerin-and-water mixture (boiling-point pure glycerin, 290° C.). In general, one can substitute for the higher temperatures a lower temperature for a longer period of time.

A simpler method later recommended by Ehrlich is to place a copper plate horizontally upon a stand, and to heat one end with a flame. After a short time each individual portion of the plate will remain at a uniform temperature, the part nearest the flame hottest, the more distant portions less so. The spot upon the plate is determined where a drop of oil of toluol just boils, without presenting *Leidenfrost's phenomenon*.[1] The cover-glass, after being dried in the air, is placed at this spot. The temperature is about 111° C. (with barometer, 760 mm.). It should remain here from one-half to one minute if ordinary stains (hematoxylin, eosin, triacid) are to be used. With many other stains the cover-slip must be left there longer or a higher temperature employed.

Rubinstein [2] recommends more intense heat even for the triple stain. For this purpose he places the cover-slip face down for one-half to three-quarters of a minute, at a spot on the copper plate where a drop of water still shows Leidenfrost's phenomenon, and in such a way that a corner of the glass reaches over toward the cooler end of the plate.

This method of fixation acts more strongly than that in which toluol is employed as above described, and gives, according to Rubinstein (for triacid), more beautiful and constant results.

There are, however, objections to the use of the copper plate in fixation, for if it be used at high temperature, the time for fixing a cover-glass smear is so short that the errors of fixation may become very numerous if the time of fixation be allowed to vary in the slightest degree. On the other hand, the plate is less adapted for

[1] The drop runs around without wetting the copper.
[2] Zeit. f. wiss. Mikros., 1897, vol. xiv, p. 456.

uniform fixation at lower temperatures, with long-continued action, because the temperature of the plate varies considerably during a period of time over a very few minutes. The upper surface of the plate eventually oxidizes and becomes uneven, and as the cover-glass does not then lie flat on the metal, the action of heat is considerably altered and the duration of the period of fixation must be modified accordingly. The author does not, therefore, recommend the copper plate method, for concordant results are obtained only by those who are devoting their entire time to this work and have consequently attained a certain facility in handling the plate. He does, however, recommend the toluol oven for general use.

The fixation depends not only upon the stain employed, but also upon the strength of the stain, and the latter varies with age, so that no absolute rule can be laid down, and frequently a satisfactory result is obtained only after several trials. In general, it can be said that weaker fixation is sufficient for eosin-hematoxylin and eosin-methylene-blue (Jenner, May-Grünwald), as well as for the Giemsa stain, while a stronger fixation is necessary for Ehrlich's triacid stain (at the boiling-point of xylol, or at the point of Leidenfrost's phenomenon of water on the copper plate for one-half to one minute, one to two hours in toluol oven, or one-quarter of an hour in the xylol oven).

Preparations may also be fixed by immersing them for five minutes in absolute methyl-alcohol, or by immersing them in a 1 per cent. solution of formalin for about one minute. With the latter, however, and with acetone the author has never had good results. Since methyl-alcohol is very hygroscopic, the fixation should be carried on in vessels with air-tight stoppers.

We must also mention here the method of fixation by osmium vapor, described on p. 682, and found by Posner to be useful for blood-smears as well as urine sediment. The author, however, still lacks several facts regarding the usefulness of this last method. After fixation, the staining of the dry smear may be postponed for some time,—one to two days,—but it is better to avoid such long delay if possible.

GENERAL REMARKS ON STAINING AND EXAMINING OF DRY SMEARS

The dry smears may be stained either by single dyes, as methylene-blue, hematoxylin, or eosin, or in several colors, by the successive action of different dyes, or by different dyes made up in mixtures or in chemical combination. In the latter case a polychromatic picture is obtained by one staining process. The method of combined stains has been adopted more and more on account of the beautiful pictures which they produce. They accomplish more than the stain made up of a single dye, are less influenced by varying conditions, and are easier than any of the successive staining methods. To stain a cover-glass smear, we can either place the fixed smear in a glass containing the stain, or if we wish to save the stain, the glass is placed in the bottom of a watch-glass with the smear side downward, and the stain is allowed to flow under it, or the cover-glass can be taken up in a Cornet clamp while lying on the table and held horizontally, the stain being dropped on the smear. This latter procedure can be employed only for staining processes of short duration, for the stain would eventually evaporate, with the formation of a precipitate which would destroy the specimen. In staining preparations on a slide we can either place the slide in the stain or drop the stain on the slide, according to the time required for staining. In the former case, to prevent precipitation, we place the slide vertically in

a tall glass, or, even better, place it smear side down on the staining solution, or we can place it horizontally, supported at both ends on small pieces of glass in a dish with the smear side down, so that the solution touches only the smear surface. It is more convenient and more economic to drop the stain on the slide when only a short time is needed for staining. Peculiarities in the technic of staining (as, for instance, in staining with the Giemsa solution) should be carried out according to the directions given for the individual methods. After staining, the blood preparations are generally washed in water, then dried with filter-paper, the drying being completed by leaving them for a moment in the air at room temperature or near a flame. They are then either examined in xylol or, if the preparation is to be saved, mounted in neutral Canada balsam. Smears are generally examined with an immersion lens, using a widely opened diaphragm. In using slide smears it is unnecessary to cover the smear with a glass for the purpose of examination, for the immersion oil can be placed directly upon the smear. To preserve for further use the immersion oil can be washed off with xylol, which dries quickly, and the specimen either mounted in Canada balsam, or put aside dry, without any covering. These dry, uncovered smears are more durable than those mounted in Canada balsam.

The dyes used in blood-staining should be obtained from the firm of Grübler, chemical laboratory, Bayrische Strasse, Leipsic, because it has specialized in these products, and very nearly approaches a faultless manufacture of dye-stuffs. In reference to the theory of staining, the author recommends Ehrlich's original paper [1] in the Encyclopedia of Microscopic Technic by Ehrlich, Krause, Mosse, and Rosen (Berlin, 1903), and the outline on the chemistry of dyes by Pappenheim (Berlin, 1901). The author describes in the following paragraph only the best of the countless numbers of recent methods for staining the blood that have been used in his clinic, and earnestly advises those who undertake to learn the technic of blood-staining, to limit themselves to these methods as they suffice for all that has, up to the present time, been found in the blood by means of stains. The continuous experimenting with new methods which have no advantage over those that are older and more tried has caused immeasurable harm, for it has frequently led to totally erroneous explanations of blood-findings and to much confusion as regards the designating of the individual elements of the blood, which are usually easily understood and recognized with the older tried methods.

Rieder's Eosin-hematoxylin Stain.—A simple method, which usually suffices for recognizing the coarser relations, consists in immersing the specimen in a saturated solution of eosin in 5 per cent. carbolglycerin for several hours (Rieder). The color is then washed off with water, and it is counterstained for a minute with 50 per cent. Delafield's hematoxylin.[2] After repeated washings, the preparation is dried in the air and mounted in Canada balsam. The red blood-corpuscles and eosinophilic granules are stained red, nuclei and cell membranes dark blue, and the protoplasm of the white cells violet or reddish. (See Pl. 8, Figs. 4 and 5.)

[1] Especially Ehrlich, Farbenanalytische Untersuchung zur Histologie und Klinik des Blutes, Berlin, 1891.

[2] Two solutions: (*a*) 1 gm. of a crystalline hematoxylin dissolved in 6 cc. of absolute alcohol; (*b*) 15 gm. of alum ammoniate dissolved in 100 cc. of distilled water, and filtered after cooling. These solutions are mixed in an open dish, and exposed to light three days. The mixture is then filtered, and mixed with 25 cc. of pure glycerin and 25 cc. of methyl-alcohol. After three days this mixture is filtered and kept in stock.

To recognize the finer details of the nuclear structure, and especially of the mitoses, Rieder recommends that blood-films be first fixed, and then immersed in a saturated aqueous solution of picric acid. They should then be washed for one or two days in running water, and stained several hours with a very dilute Delafield hematoxylin; then washed in water again, and finally in water containing hydrochloric acid, dried in the air, and mounted in Canada balsam.

Ehrlich's triacid stain is usually employed when examining for Ehrlich's granules. This is prepared in the following way:

Saturated aqueous solution of orange-G, 120 to 125 cc.; saturated aqueous solution of acid fuchsin, 80 to 165 cc.; saturated aqueous solution of methylene-green, 125 cc.; water, 300 cc.; absolute alcohol, 200 cc.; glycerin, 100 cc.

These solutions are generally dropped on the fixed, dry smear. To stain cover-glass preparations, and at the same time to prevent precipitation, Rubenstein places a drop of the triacid solution on a slide and lays the fixed smear down on it. After staining from five to seven minutes, the smear is washed in water, dried with filter-paper, and mounted in Canada balsam.

Precipitates almost always form in time in triacid solution, and if any of the precipitate be placed on the smear, it interferes with the picture. It is, therefore, advisable to avoid shaking up the bottle containing the triacid solution, and it is better to take the solution from the bottle by means of a finely drawn pipet and drop it on the smear. Rubenstein's method, described above, also prevents the disturbing action of the precipitate to a large extent. By frequent filtering the staining power of the solution may be diminished, and rather than filter, therefore, it is advisable to allow the solution to stand for a few days until the precipitate settles, if in any way it was accidentally shaken up.

Plate 6 shows the various elements of the blood stained with triacid.

The neutrophile granules appear most beautifully stained with triacid. The hemoglobin takes on an orange to a brownish color (Pl. 6, Fig. 1, No. 8). The nuclei are bluish green; the neutrophile (ϵ) granules violet (Pl. 6, Fig. 1, No. 1); the eosinophile (a) granules copper colored (Pl. 6, Fig. 1, No. 2). The protoplasm of the lymphocytes and large mononuclear cells is unstained, or after strong fixation, a pale pink (Pl. 6, Fig. 1, Nos. 5–7). The basophile granules of the red blood-cells are unstained, just as the basophile granules in leukocytes. The latter can at times be recognized as colorless spaces (Pl. 6, Fig. 1, No. 3). The large mononuclear cells often show a light, violet-reddish, neutrophile granulation. (See p. 789.)

Successful triacid smears can be obtained only after strong fixation, either by long-continued hardening in methyl-alcohol or by strong heat fixation. (See p. 774.) The triacid solution is, on the whole, durable. Solutions which are too old, however, frequently act improperly, and must then be replaced by fresh ones.

The author cannot here sufficiently emphasize the importance of using the triacid solution in all doubtful cases. As regards the determination of neutrophile granules, which are equally important clinically as well as physiologically, the triacid stain is second to none, and the replacement of this stain by the newer ones, such as Jenner's and Giemsa's, which require less fixation, has led to many erroneous results, inasmuch as these methods, though they frequently give good results, may, as in some cases in the author's experience, leave one in doubt, for as yet unknown reasons, since they do not bring out the neutrophile granules clearly enough. This frequently leads clinical assistants with little experience to totally erroneous results, since, for instance, lymphocytes and myelocytes may be mistaken for one another, or it may be assumed that the neutrophile cells or the myelocytes are deficient in neutrophile granules, etc. For these reasons, in a clinic where assistants with little experience often work, the rules for triacid staining must be implicitly adhered to and the technic must be thoroughly mastered.

Panoptic Triacid Stains and Nuclear After-staining of Triacid Preparations.—Since the nuclei in triacid preparations appear but slightly stained, Pappenheim [1] has described a so-called panoptic triacid mixture, in which the methyl-green is replaced by methylene-blue. This can be obtained from Dr. Grübler in Leipsic, in a solution ready for use. By means of this solution the nuclei are better stained; the granules are, however, not so distinct as with the original triacid. It is, therefore, recommended to restain the Ehrlich triacid preparation with a dilute 0.25 per cent. watery methylene-blue solution in case a better nuclear stain be desired. We then obtain a good staining of mast-cell granules, besides a good nuclear stain.

Staining the Blood with Methylene-blue.—As a stain we may use a 0.25 to 0.50 per cent. watery methylene-blue solution (methylene-blue "pure," Höchst) or Löffler's alkaline methylene-blue, which can be obtained by mixing 0.5 gm.

[1] Deut. med. Woch., 1901, No. 46.

methylene-blue in 30 gm. of alcohol with 1 cc. of a 1 per cent. potassium hydroxid solution and 100 cc. of water. Well-fixed preparations are stained only for a short time (about five seconds) in using Löffler's methylene-blue, and then immediately washed off with water. The methylene-blue also serves for the determination of bacteria and malarial plasmodia (see p. 818), and especially for the recognition of polychromatophilia and basophilic granulation of the red blood-cells. While the normal red blood-cells appear yellowish green after proper fixation, the polychromatophilic cells present may be recognized by their greenish-blue or even pure blue shade. The term polychromatophilia is not strictly correct in speaking of the preparations stained with a single dye: one should rather speak of a more or less high grade of basophilia. The red blood-cells containing basophile granules appear with pure methylene-blue stain, dotted with blue, as is the case with the combined stains (Pl. 4, Fig. 4, *a*, et seq., and Pl. 5, Fig. 2, No. 27); but the granules seem to rise up from a yellowish-green rather than reddish background. The neutrophile and eosinophile granules of the leukocytes are unstained, the basophile granules blue, or with certain varieties of methylene-blue they are violet. (See Giemsa's stain.)

The Jenner Stain.—This method has been largely adopted because of its convenience, since with it special fixation before staining is unnecessary. It depends upon the employment of a chemical compound of methylene-blue as a base and eosin as an acid. This compound stains the blood elements more or less selectively, partly blue, partly red, and partly with a mixed color. There is practically no difference between Jenner's original method and that employed by May and Grünwald. The methods of procedure which have led up to the use of the combination stain are to be found in the older editions of this work, and cannot be entered into here, but the author recommends in this connection the work of Türk.[1] The possibility of staining smears without previous fixation depends upon the fact that the dye is dissolved in methyl-alcohol, and dyeing and fixing occur, therefore, at the same time. The dye may be obtained from Grübler, either in powdered form or solution. Burroughs, Wellcome & Co., of London, also prepare compressed tablets of this, which are to be dissolved in 10 cc. of methyl-alcohol. If the powder be used, 0.3 gm. should be dissolved in 100 cc. chemically pure absolute methyl-alcohol. As methyl-alcohol cannot always be obtained pure, the author recommends Dr. Grübler's stock solutions.

According to Jenner's original directions, the stain is dropped on the unfixed, air-dried, and, for the best results, freshest possible smear. If a cover-glass be used, it should be held in a Cornet clasp. After allowing the stain to remain on for two to three minutes, the preparation is rinsed in distilled water for five to ten seconds, until the color of the smear is pink. The preparation is now dried quickly with filter-paper, then with slight heat, and mounted in Canada balsam, or if it be a slide preparation, examined directly in cedar oil. In older smears, or in those that stain with difficulty, the author recommends that the specimen be first fixed in absolute methyl-alcohol for ten to twenty minutes; then stained with a mixture of 1 part stain and 2 parts distilled water for five to fifteen minutes: then proceed as above. If the staining cannot be undertaken immediately after fixation, the author suggests that the preparation be dried and put in a desiccator over calcium chlorid, *i. e.*, kept absolutely dry until staining is begun.

To eliminate certain difficulties which arise at times in the Jenner method the technic has been modified so that after three minutes' fixing and staining with the concentrated solution an equal amount of distilled water is added and staining is continued for five to fifteen minutes. Then proceed as above. A further modification of the Jenner technic, that of Assman, Jr., has given very good results in the author's clinic. The directions are as follows:

(1) Place the slide with the blood-smear still unfixed in a perfectly clean Petri dish and cover with 40 drops of the methyl-alcohol stain, so that the latter does not overflow the edge of the slide. This is left on the smear for three minutes for purposes of fixation.

(2) Add 20 cc. of distilled water to which 5 drops of a 1 per cent. potassium carbonate solution has been added, and shake the dish until a uniformly clear, light-violet, watery solution is obtained which is free from precipitate; allow this staining process to go on for five minutes.

(3) Remove the preparation and dry without further rinsing. Place in Canada balsam, or, if a slide preparation, examine directly in cedar oil.

The smears pictured in Pl. 4 and Pl. 5, Fig. 1, are stained according to Jenner. In general, if well done, they are not at all inferior to the triacid preparations. One

[1] Türk, Vorlesungen über klinische Hämatologie, Wien, 1904.

advantage over the triacid is that they show a good nuclear stain of the leukocytes and red blood-cells. The basophilic granulations of the leukocytes appear deep blue (just the opposite of the triacid stain) (Pl. 4, Fig. 2, *g*, and Pl. 5, Fig. 1, *e*), or frequently, depending upon the dye used in the preparation of the solution, even metachromatic violet, on account of the azure content of the methylene-blue. (See Giemsa's stain.) The neutrophile granules of the leukocytes are stained reddish violet (Pl. 4 and 5, Fig. 1), and we readily recognize, from their bluish tint, the polychromatophilic red blood-cells and the deep-blue basophile granulations of the "stippled" erythrocytes (Pl. 4, Fig. 4, *a*, etc.). The normoblasts (Pl. 4, Fig. 4, *b*, and Pl. 5, Fig. 1, *h*) show an intensely stained black-blue nucleus, while in the megaloblasts it is a paler blue (Pl. 4, Fig. 4, *d*, and Fig. 1, *g*). The nucleus of the lymphocytes (Pl. 4, Fig. 4, *h–n*) appears darker when weakly fixed, and lighter when strongly fixed, than the surrounding protoplasm (Pl. 5, Fig. 1, *g*). The large mononuclear cells show a slightly basophilic protoplasmic reticulum (Pl. 4, Fig. 40).

In spite of the advantage of good Jenner's preparations, the author states that the advantage of this procedure cannot always be realized, for some unknown reason. There are cases where, probably on account of the stain or the preparation of the smear, the neutrophile granules are unstained or insufficiently stained, in which case they are of a bluish shade, and cannot be readily distinguished from the surrounding protoplasm. The experienced worker will, without further ado, discard this smear in these cases and resort to the triacid stain. With the inexperienced worker, however, the use of such preparations may give deceptive results, on account of the insufficient staining of the neutrophile substance, with consequent confusing of neutrophile and basophile granules. This peculiarity of the stain prevents its universal employment, and for this reason the author recommends supplementing the Jenner by the triacid stain, in cases of even the slightest doubt. Frequently the above-mentioned faults of the Jenner method can be eliminated by energetic heat fixation before staining (ten minutes to one hour in the toluol oven). In many cases the author obtained satisfactory results in this way. By strong fixation we bring about the ready recognition of the lymphocytes and their differentiation from the large mononuclear cells, for in strongly fixed preparations the protoplasm of the lymphocytes is stained more deeply with methylene-blue than the nucleus, while the large mononuclear cells behave exactly the opposite. The difference in the nucleated red blood-cells is also brought out. (See pp. 788 and 789.)

Giemsa's Stain.—There are certain forms of methylene-blue that are not strictly pure, but contain, in addition, a red dye. Romanowski first made use of this kind of methylene-blue especially for the staining of malarial plasmodia. This dye, however, gave uncertain and unreliable results until Giemsa employed it as the so-called azure dye (which is obtained from methylene-blue by the special method of Michaelis) in combination with eosin and methylene-blue. This is the dye which in older methylene-blue and certain Jenner solutions showed the metachromatic violet stain of the mast-cell granules. The Giemsa solution is made up of methylene azure with eosin and methylene-blue in alcohol and glycerin. It is quite difficult to prepare it, and it is better to obtain a stock solution from Dr. Grübler in Leipsic. The staining is carried out as follows: the air-dried smear is fixed for one-half hour in absolute alcohol, preferably absolute methyl-alcohol. A dilution of the Giemsa solution is then prepared just before using by mixing 4 drops of the solution in 4 cc. of distilled water at 40° C. The smear is then covered with the uncooled solution, which is left on for thirty minutes. The solution being warm at first, the most favorable time is used for fixing the smear, as some of the dye is precipitated during cooling. In order to avoid these interfering precipitates it is better to place the cover-glass preparation in a watch-glass or a concave dish, with the smear face downward in stain, for in this way the precipitate cannot settle on its surface. Similarly, it is recommended that the smears on slides be placed with the diluted and warm solutions in a covered Petri dish, with the smear on the under surface, the ends of the slide resting on fragments of glass. In this way a faultless specimen is obtained. After the staining is complete, the preparation is rinsed in water, dried with blotting-paper, then with slight heat, and, if a cover-glass, mounted in neutral Canada balsam, or if it be a slide preparation, examined directly with the immersion lens in cedar oil without a cover-glass. The Giemsa stain (see Pl. 5, Figs. 2 and 3) gives generally beautiful panoptic views, whichsdo not, however, have such markedly different colors as either the Jenner or triacid stain, but it suffices for diagnostic purposes, and in a differential leukocyte count offers the advantage of a very intense staining of the white cells. (See p. 794.) The most

important blood elements are shown with the Giemsa stain in Pl. 5, Figs. 2 and 3. The nuclei appear violet, the mast-cell granules partly unstained, partly violet black (Pl. 5, Fig. 2, Nos. 3 and 4), the basophile granules of the red blood-corpuscles are blue (Pl. 5, Fig. 3, No. 27), the neutrophile granules of the polynuclear leukocytes are pale to dark violet (Pl. 5, Fig. 2, No. 1), the eosinophile granules are red (Pl. 5, Fig. 2, No. 2), the protoplasm of the lymphocytes and transition cells (Pl. 5, Fig. 2, Nos. 10–13 and 5 and 6) is blue to violet, that of the large mononuclears, blue to bluish violet (Pl. 5, Fig. 2, Nos. 7–9), the red blood-corpuscles reddish, the polychromatophilic red cells are bluish red (Pl. 5, Fig. 3, Nos. 26 and 28). The azure granules visible with this stain as violet to red dots in many lymphocytes are particularly confusing to beginners (Pl. 5, Fig. 2, No. 10), and may lead to mistaking myelocytes for lymphocytes.

The Giemsa method, like the Jenner, is somewhat unreliable as regards the staining of neutrophile granules. The author believes that the Giemsa method is very useful, but that it can in no way replace the others, as being universally preferable, and that it is one in which the inexperienced must observe certain precautions.

Leishman's Stain.[1]—In principle this is the same as Giemsa's, and has the advantage that it is easier and can be carried out more quickly. A stock Leishman stain, containing methylene-blue, eosin, and azure, can be obtained from Dr. Grübler, or can be prepared by dissolving 0.2 gm. of the powdered dye, or one of the tablets prepared commercially by Burroughs, Wellcome & Co., of London, in 10 cc. of absolute methyl-alcohol. Fixation is accomplished at the same time as the staining by the methyl-alcohol, just as with the Jenner stain. The technic is as follows: The air-dried, unstained smear is covered with the stain. After one minute an equal up to double the quantity of distilled water is added and is carefully mixed by gently moving the slide backward and forward. The diluted solution is left on the smear for five minutes, washed with ordinary water, dried with blotting- or filter-paper, then with gentle heat, and mounted in Canada balsam or examined in cedar oil.

The results from the Leishman stain are just the same as with the Giesma method, only the basophile granules of the mast-cells are more constantly stained on account of the alcoholic solution of the dye. The ideas of the author as regards the exclusive use of the Giesma method are also applicable here. (See above, Giemsa's Stain.) Excellent smears stained exactly according to Leishman are shown in large numbers in the Atlas of Blood Diseases by Schleip (Berlin, 1907, Urban and Schwarzenberg).

The Pyronin Methyl-green Stain of Pappenheim.[2]—A stock stain can be obtained from Dr. Grübler. It contains two basic dyes of different combining powers. Pyronin is a much stronger base than methyl-green. It stains red the strongly basophile substances, as the protoplasm of lymphocytes and Türk's irritation forms (plasma cells), and, according to Nägeli, the small myeloblasts, as well as the strongly polychromatophilic red blood-cells. According to Nägeli, a cell is not a lymphocyte unless its protoplasm stains red with pyronin, but it does not hold that all cells whose protoplasm is red are lymphocytes. Smears treated with pyronin methyl-green are best fixed by heat, then stained for five minutes with the prepared dye, washed off, dried, and mounted in Canada balsam, or examined directly in cedar oil.

[Hastings[3] has devised a permanent Nocht stain which is used in solution in methylic alcohol. The preparation of the staining fluid is somewhat difficult. It had best be secured from Ernst Leitz, 30 East 18th St., New York City.

To use the stain no previous fixation is necessary. The dried smear is flooded with the staining fluid for one minute; the solution is then diluted with 5 to 7 drops of water; and this diluted stain is allowed to act for five minutes. The specimen is then washed in distilled water, care being taken to clean off the negative side of the glass upon which a precipitate collects, blotted with filter paper and examined directly or mounted in balsam.

All the leukocyte granulations are well differentiated. The granular basophilic and polychromatophilic changes in the red cells are well shown, and the blood-plates stain clearly.—Ed.]

[1] Leishman, Brit. Med. Jour., September, 1901, xxi.
[2] Virchow's Arch., 1899, vol. clvii.
[3] Hastings, Jour. Exper. Med., 1905.

IODIN REACTION AND GLYCOGEN CONTENT OF THE LEUKOCYTES

Ehrlich's methods are the best for demonstrating the *microscopic iodin reaction of the blood.* The dried blood-film (which must, however, not be heated) is immersed in a solution of iodin and gum arabic (iodin 1, potassium iodid 3, water 50, and enough gum arabic to render the fluid thick). Ehrlich [1] has since announced that it is an advantage to substitute iodin itself for the solution of iodin. This is done by placing the preparations dried in the air under a closed glass containing crystals of iodin for several minutes, until the color is dark brown. The preparation should then be examined in a saturated syrupy solution of levulose; and to preserve it, should be surrounded with varnish. The color of the leukocytes varies in individual cases. The red blood-cells are stained diffusely brown, although this, at present at least, has no special interest. Zollikofer has established the following facts with regard to the leukocytes.[2] Under physiologic conditions, brown-stained protoplasmic granules are found most frequently in lymphocytes, oftentimes in mast-cells, and exceptionally in the large mononuclear cells; the polynuclear neutrophilic cells are faintly stained brown. A distinct deposit of brown-stained granules and flakes in the last-mentioned cells is considered pathologic. This condition is the one which writers have paid most attention to up to the present time. It is ordinarily spoken of as the *iodin reaction* of the leukocytes or the *intracellular iodin reaction of the blood. Zollikofer's brown granules* are very rarely found in eosinophiles, and then under conditions which are not understood or defined. They are never found in the neutrophilic mononuclear cells (myelocytes). Ehrlich[3] has also described a so-called extracellular reaction, in which stained brown, granular masses are found outside of the leukocytes. Gabritschewski [4] and Zollikofer have shown, however, that these formations are blood-plates, which, under conditions not definitely known, give the iodin reaction, at times in normal blood, at times under pathologic conditions, especially in diabetes mellitus. This reaction does not necessarily accompany the intracellular reaction.

According to the findings of Zollikofer, it has been conclusively shown that if iodin vapor be allowed to act on moist smears, the iodin reaction is greatly increased, so that in perfectly normal blood we may find fine brown granules instead of the diffuse light-brownish color in the neutrophile leukocytes. The absence of these normal granules in dry smears treated with iodin is due, according to Zollikofer, to the destruction of the granules in the normal cells occasioned by the drying. In pathologic accumulations of this iodin-staining substance the destruction of the granules by drying is not sufficient to make them disappear entirely. The term "positive iodin reaction," or "iodophilia," can, therefore, only be employed in expressing the results on dry smears obtained by Ehrlich's method, as above described.

This brown-staining substance is generally supposed (and by Ehrlich, too) to be glycogen. But Czerny,[5] Kamminer,[6] and especially Zollikofer, discredit this theory. Very likely it is related to amyloid. Under certain conditions it is stained violet and not brown by iodin, which favors this latter view.

The pathologic iodin reaction, at present at least, applies only to the appearance of brown-stained granules in the polynuclear neutrophiles. Very little can be said as yet in regard to the clinical significance of this "iodin reaction." It is almost always present with *leukocytosis,* especially in purulent conditions, but not, for instance, in erysipelas.

According to the investigations of Zollikofer in the Bern Clinic, the presence of this reaction (*e. g.*, in appendicitis) does not always prove the presence of pus, neither does its absence exclude the presence of pus. About the same results were observed in cases which recovered spontaneously and in those which came to operation. No definite conclusions can be drawn from the absence or presence of the iodin reaction in diabetes mellitus, although several observations of Zollikofer's would seem to indicate that a diminution of diabetic acidosis is associated with diminution of the reaction. It was thought that the reaction might possibly be used in the diagnosis of amyloid degeneration, an opinion based upon the observations of Czerny relative to the presence of the iodin reaction in artificially produced amyloid degeneration; but observations in the author's clinic have disproved this. Zollikofer found

[1] Ehrlich and Lazarus, Die Anämie, Nothnagel's spec. Path. u. Therap., 1898.
[2] Zur Iodreaction der Leukocyten, I. A. D., Bern, 1899.
[3] Zeit. f. klin. Med., 1883, vol. vi.
[4] Arch. f. exp. Path. u. Pharm., 1891, vol. xxviii.
[5] Ibid., vol. xxxi.
[6] Deut. med. Woch., 1899, vol. xv.

that if iodin vapor acted upon moist preparations, the reaction was considerably increased, so that even in normal blood fine brown granules appeared in the neutrophilic leukocytes, instead of the diffused light-brown stain. The absence of these normal granules in the dry specimens treated with iodin is due, according to Zollikofer, to the disintegration of the granules in the interior of the cells during the process of drying.

Best's glycogen stain,[1] by means of carmin, ammonia, potassium carbonate, and methyl-alcohol, which gives wonderful results in sections, cannot, unfortunately, be employed for dry smears, according to the studies of Dr. Wegelin. This ought to be a new and important fact, according to Zollikofer and others, in differentiating the brown, iodin-staining substances of the leukocytes from the glycogen.

From the more recent observations on the clinical significance of the iodin reaction we find the following: In typhoid, the iodin reaction is negative (Hofbaur); also in malaria (Huber, Hofbaur); in articular rheumatism (Sorochowitsch), and in tuberculosis (Hofbaur), if these be not complicated by mixed infection. As a point in differential diagnosis between articular rheumatism and general gonorrheal infection it is noteworthy that the latter is attended by iodophilia (Sorochowitsch).

MICROSCOPIC EXAMINATION OF THE ALKALI DISTRIBUTION IN THE BLOOD, ACCORDING TO EHRLICH AND LAZARUS

This method[2] depends upon the fact that iodoeosin (the free acid) in chloroform solution will stain the alkali part of the dry blood-smear a deep red. If we place a dry blood smear without fixation in such a solution, it quickly becomes of a deep-red color. If this be now washed with chloroform and placed in Canada balsam while still moist, the plasma will appear red, the red blood-corpuscles colorless, the protoplasm of the white blood-cells red, while the nuclei will appear as colorless spaces (negative nuclear stain). Fibrin will also appear intensely red. This theoretically interesting stain has been found of but little value to date.

MICROSCOPIC APPEARANCE OF ERYTHROCYTES

(Poikilocytosis; Staining Capacity of the Red Blood-cells; Polychromatophilic Changes; Granular Basophilic Degeneration)

The red cells or erythrocytes are normally biconcave disks. Under pathologic conditions, however, they may present very abnormal shapes, a condition which has been called by Quincke poikilocytosis. Poikilocytes may assume any shape (see Fig. 307 and Pl. 8, *a*, Fig. 1, *c*). Their size, too, may vary considerably. Poikilocytosis is observed in all cases of *grave anemia*, especially in the so-called *pernicious types*, in *leukemia*, in the *cachexia* of *carcinoma of the stomach*, and rarely in the innocent types of anemia, such as *chlorosis*. The diagnostic significance of poikilocytosis is not so great as was formerly supposed. It certainly is by no means pathognomonic of pernicious anemia. As a rule, the degree of poikilocytosis corresponds to the degree of oligochromemia.

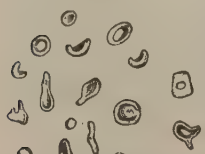


Fig. 307.—Poikilocytes in pernicious anemia.

Maragliano[3] considers these degenerative types of red blood-cells. Thus, if normal blood be examined under a cover-glass fixed to a slide with paraffin at the temperature of about 26° to 27° C., a number of progressive changes occur in the corpuscles, and these same changes are found in the fresh blood under pathologic conditions. After thirty to seventy minutes the so-called *endoglobular changes* occur. A colorless region, irregularly outlined, develops from the center and shows

[1] Zeit. f. wiss. Mikros., 1906, vol. xxiii.
[2] Ehrlich and Lazarus, Anemia in Nothnagel's System.
[3] Zeit. f. klin. Med., 1892, vol. xxi, p. 419.

an ameboid motion. (See Plate 7, Figs. 18–22.) Considerably later—three to four hours—so-called total alteration of the blood-cells begins, and the external shape is changed. This change commences with the formation of a thorn-apple or mulberry-like appearance, which, according to Maragliano, has incorrectly been considered to be the result of drying. The blood-corpuscles gradually become more and more deformed (ten to twelve hours); pseudopodia develop with an ameboid-like motility very much like that of the decolorized spots above described. Poikilocytes are formed in this way. Maragliano has called attention to the fact that not only poikilocytes, but all the other types of degeneration described, especially the crenated types of blood-cells, may be found in the fresh preparation of severe blood-diseases. Less serious pathologic changes of the blood manifest themselves by the fact that these changes take place outside of the body sooner than in normal blood-specimens.

These changes have diagnostic value only when they are seen in absolutely fresh specimens. Pressure on the tissues when removing the blood and on the cover-glass must be avoided, because this may produce artificial deformity of the blood-cells. On the other hand, the abnormally rapid appearance of deformity in blood apparently normal on removal indicates a certain lack of resistance of the red cells, and is not entirely without diagnostic interest. The crenated types are of especial interest in this respect, although they have not yet been studied from a clinical standpoint.

We must, however, be very careful in considering these as postmortem changes, for they may also appear in the normal blood under extremely unfavorable conditions, brought about by rapid drying. The inexperienced should, therefore, put little value on crenated forms.

BEHAVIOR OF THE ERYTHROCYTES TO STAINS; ANISOCHROMIA; POLYCHROMASIA; BASOPHILIC GRANULATION OF THE RED BLOOD-CORPUSCLES

So far as the staining capacity of the red blood-corpuscles is concerned, the dry preparations take acid stains very readily (eosin, orange-G). The intensity of this stain depends upon the amount of hemoglobin contained in the cells. This is of practical importance, because after a little practice the degree of anemia or oligochromemia can be made out from dry specimens. The difference between normal red cells and those deficient in hemoglobin is much more striking in the stained dry preparation than in unstained cells.

Unequal hemoglobin content of the individual red blood-corpuscles (anisochromia, see p. 771) can be well recognized in stained smears by the difference in the intensity of the stain of the erythrocytes.

The so-called vital staining of the red blood-corpuscles with certain dyes, *e. g.*, neutral red, which can be carried out by adding the stain directly to the fresh smear, depends apparently upon the degeneration of the red blood-corpuscles. Since they have no practical value, these so-called vital stainings, which are in no sense vital, cannot be discussed here. Living red blood-corpuscles are achromatophilic and cannot be stained by any dye. If the red blood-corpuscles are fixed by drying and heating, they take up the eosin and chemically related (acid) dyes.

Degeneration of the red cells described by Maragliano may be demonstrated by staining. (See p. 782.) Endoglobular degenerated blood-cells devoid of color in the center (see above) do not act in this way. The decolorized portion in dry preparations stains with hematoxylon, whereas the peripheral region, containing hemoglobin, stains with eosin. To demonstrate this, the eosin-hematoxylin staining methods described upon p. 776 may be employed. The fact that the endoglobular region stains proves that it is not a vacuole, as was formerly believed, a view which is still held by some authorities.

Polychromatophilia consists in a change in the staining capacity of the red cells. Normally shaped red cells, as well as poikilocytes, which normally take the acid components from staining mixtures, are tinged with the methylene-blue (Jenner's stain, see p. 778 et seq.)

or eosin hematoxylin (p. 776) present therein, the tint varying from eosin-red, with a bluish tinge, to pure violet. Polychromatophilia is most distinctly brought out by using plain methylene-blue (see p. 778)—best, Löffler's alkaline methylene-blue after good fixation. Normal red cells then appear pale yellow or, at the most, greenish. The polychromatophiles appear green to blue.

This change has been noticed in nucleated red cells, especially the megaloblasts in pernicious anemia (see p. 787 and Plate 4, Fig. 4 *c*, Plate 5, Fig. 3, No. 26) and, like poikilocytosis, is found in all severe cases of anemia. Occurring under such conditions, it is suggestive of degeneration, and was, therefore, described as such by Ehrlich and Gabritschewski. This view, however, has become untenable, since we know that polychromatophilic staining is present in the early developmental stages of erythrocytes. It could be imagined quite as easily that the polychromatophilic changes were indicative of processes of regeneration.

Another peculiar change is the so-called *granular* (*granular basophilic*) *degeneration of the erythrocytes*. (Basophilic granulation, stippling of the erythrocytes.) This has been closely studied by Lazarus, Askanazy, Plehn,[1] Grawitz,[2] Nägeli, and others. In specimens stained with Jenner's, Giemsa's, or Leishman's solutions, or by brief immersion in Löffler's methylene-blue [3] (see p. 777), some of the erythrocytes are seen to contain a number of blue to bluish-black (basophilic) granules. (See Plate 4, Fig. 4 *a;* Plate 5, Fig. 3, No. 27.) This change has been found chiefly in conditions associated with destruction of the erythrocytes, such as pernicious anemia, leukemia, certain forms of tropic anemia, carcinoma, chronic lead-poisoning, sepsis, and malaria. Basophilic granulation is of the greatest diagnostic importance in the recognition of chronic lead-poisoning (Nägeli). The statement of Grawitz, that granular basophilic degeneration has never been found in chlorosis, has not been confirmed. Rosin and Biber state that they have observed basophilic granules in the erythrocytes of healthy individuals. Grawitz succeeded in producing this change in mice by overheating the animals. Lazarus and Askanazy look upon the basophilic granules as the remains of disintegrated nuclei ("karyolytic fragments"), but Grawitz attributes them to degenerative changes in the stromata of the erythrocytes. Most other recent writers, on the contrary, correctly regard the basophilic granulation as a phenomenon holding some relation to the regeneration of the blood. Jawein,[4] for instance, observed this change in a patient recovering from a bothriocephalus anemia. Nägeli also regards it as a sign of regeneration, basing his opinion on Pappenheim's demonstration of basophilic stippling in cells from normal bone-marrow, on Engel's and Schmidt's finding of the same in embryonic blood, and on his own clinical observations that in the severest grades of lead-poisoning the basophilic granules disappear, whereas, with the improvement of the anemia, they again occur. Nägeli also demonstrated that in experimental lead-poisoning in animals recovery following the use of potassium iodid is accompanied by marked basophilic stippling. It is probable that basophilic granulation is intimately related to erythrocytic polychromatophilia, with which it is so frequently associated.

The question whether the granules represent nuclear remnants or are derived from the protoplasm is not yet decided. Both suppositions are consistent with the interpretation of the change as a regenerative phenomenon.

A complete exposition of the ideas on basophile granulations of erythrocytes can be found in the article by Askanazy, from Lichtheim's clinic.[5]

The larger particles staining with methylene-blue that result from the well-known nuclear destruction in nucleated red blood-corpuscles are to be distinguished from the true basophilic granulations described above.

[1] Deut. med. Woch., 1899, No. 28–30.

[2] Ibid., 1899, No. 36, and 1900, No. 9.

[3] Concentrated alcoholic solution of methylene-blue, 30.0, 0.01 per cent. potassium hydroxid, 100.

[4] Berlin. klin. Woch., 1901, p. 35.

[5] Zeit. f. klin. Med., 1907, vol. lxiv, parts 3 and 4, p. 288. See also the work of Nägeli, Münch. med. Woch., 1904, No. 5.

ERYTHROCYTIC SHADOWS [PONFICK'S SHADOW CORPUSCLES; HAYEM'S ACHROMACYTES.—Ed.]

These forms, which appear in the blood, have the shape of red blood-corpuscles, but are absolutely devoid of color, so that the central depression can no longer be distinctly recognized. They are the stromata of red blood-corpuscles which have lost their coloring-matter. They may be produced artificially if sufficient water or hypotonic salt solution to lake the red blood-corpuscles be added to normal blood. (See p. 768.) They are found pathologically wherever, by osmosis or by chemical hemolysis, red blood-corpuscles are being rapidly destroyed, as in hemoglobinuria occurring independently or as the result of poisoning with chlorate of potash or other poisons which destroy red cells. They may also be found, although in smaller numbers, in pernicious anemia. If erythrocytic shadows be present, hemoglobin may be demonstrated in the serum or plasma by adding hirudin to prevent coagulation and then centrifuging. However, the destruction of red cells may be so gradual that all free hemoglobin is straightway decomposed or excreted by the kidneys.

VARIATION IN THE SIZE OF RED BLOOD-CORPUSCLES; ANISOCYTOSIS; THE VOLUME INDEX

The true size of the erythrocytes is best determined in a fresh, unstained specimen, because drying alters their size. Even in healthy individuals the red blood-corpuscles are not all of the same size. The normal size varies, according to different authors, between 6 and 9 μ (averaging about 7). The very large cells are called giant corpuscles, or macrocytes; the small ones, microcytes. According to Gram, the red blood-corpuscles are larger in northern than in southern countries. Although slight in a normal individual, there may be very great differences in size in the same blood under pathologic conditions. This condition of the blood is called *anisocytosis*. The very large erythrocytes (9 to 16 μ in diameter) are called *giant cells, megalocytes*, or *macrocytes*. The very small ones (3 to 4 μ in diameter), *dwarf cells* or *microcytes*. There is a striking anisocytosis in pernicious anemia, in which macrocytes as well as microcytes are present. It has often been assumed that the latter signify the fragmentation of the poikilocytes. The presence of megalocytes, however, which depends strictly on the occurrence of megaloblasts, is particularly characteristic of this disease, and, according to Nägeli, of greater diagnostic import than poikilocytosis. Microcytes, on the contrary, play an important part in the secondary anemias and in chlorosis. In the latter disease megalocytes, if present, are usually pale, whereas in pernicious anemia they are, as a rule, dark red.

The Volume Index (Quotient or Value) of the Erythrocytes.—We are indebted to J. A. Capps[1] for an interesting study of the size of the erythrocytes. By means of the hematocrit and without dilution (see p. 766) this author has determined the volume of the erythrocytes as compared to the volume of the whole blood (cells + plasma). In normal cases he obtained a corpuscular volume of 50 per cent. If this value be regarded as 1, the volume in pathologic cases may be calculated in per cent. of the normal volume, just as is the amount of hemoglobin. Capps also counts the erythrocytes in the blood under observation, and expresses this number in per cent. by comparing it with the normal number of erythrocytes. By dividing

[1] Jour. Med. Research, 1903, vol. v and vi.

the volume of the erythrocytes by the number of the erythrocytes (both expressed in percentages) he obtains the so-called volume index of the erythrocytes, for which expression the author would suggest substituting "volume quotient" or "volume value" of the erythrocytes, analogous to the hemoglobin quotient or hemoglobin value [color index.- Ed.] of the erythrocytes. The volume index or quotient, therefore, measures the average volume of the individual erythrocyte. Under normal conditions, it is evidently equal to 1. Capps found that an increase in the volume index of the erythrocytes is one of the most constant and distinctive characteristics of pernicious anemia, which agrees with the well-known fact that many megalocytes are present in this disease, and that the color index is likewise greater than 1. [Capps' work is important in showing that the color index never exceeds the volume index in pernicious anemia; in other words, that the corpuscles are not supersaturated with hemoglobin. The volume index may be above the color index; it is apt to fall less rapidly from blood destruction and to return more rapidly to the normal during blood regeneration than the volume index. The high color index, therefore, depends upon the increased size of the cells. Capps found no evidence of an acute dropsy of the red cells.—Ed.] The secondary anemias, on the other hand, usually exhibit a diminished volume index of the erythrocytes. The same is true of chlorosis, in which affection a normal or slightly diminished volume index gives a good prognosis, while a markedly diminished volume index is less favorable. When utilized in this manner, the volume index is much more reliable for prognosis in chlorosis than is the hemoglobin percentage or the color index.

Capps also found that in normal erythrocytes with a volume index of 1, the discoplasm is saturated with hemoglobin, so that a color index greater than 1 indicates an enlargement of the erythrocytes. Upon the other hand, the color index may fall irrespective of a corresponding diminution of the volume index. It consequently follows that if the color index of the erythrocytes be above normal, the volume index must also be increased; while if the color index be below normal, the volume index is not necessarily diminished. The osmotic pressure of the blood-plasma should have no influence upon the volume index. The author finds this difficult to understand, and believes that it requires further investigation.

NUCLEATED RED CELLS (ERYTHROBLASTS) AND FREE NUCLEI; CABOT'S AND SCHLEIP'S RING FORMS

Nucleated red blood-corpuscles do not occur in normal blood. They may be considered as evidence of some abnormality in regeneration. They are found especially in anemic conditions. Ehrlich subdivides the nucleated red blood-cells into normoblasts and megaloblasts. The normoblasts are red blood-corpuscles about the size of normal cells, with one or sometimes several nuclei. These nuclei stain intensely with nuclear stains, such as hematoxylin, methylene-blue, Giemsa's, and Leishman's stain; and usually much more intensely than the nuclei of leukocytes or than any other nuclei. This staining quality is very characteristic, and enables us to recognize the free nuclei of normoblasts when found in the blood. Unstained, the nuclei of normoblasts appear as bright centers in the red blood-corpuscles, free from hemoglobin. They differ from the normal depression of red cells by their sharp outline, and from endoglobular degeneration in being somewhat granular (a normoblast is represented in Plate 8, Fig. 5, and in Pl. 4, Fig. 4 *b;* a free nucleus from a normoblast in Pl. 4, Fig. 4 *f*, and Pl. 5, Fig. 3, No. 29). We sometimes observe red corpuscles with two well-developed nuclei which sometimes exhibit mitoses. The nucleus of young normoblasts at times resembles the spokes of a wheel (Pappenheim). With increasing age the nucleus becomes thicker or denser (*pyknotic*), so that it is stained homogeneously and deeply. Megaloblasts are considerably larger than normoblasts—two to four times as large. The nucleus, although somewhat larger than that of a normoblast, occupies a comparatively smaller portion of the cell. It is less distinctly outlined, and does not have the same affinity for nuclear stains, so that

it is usually but very faintly stained. Staining brings out its net-like structure (see Pl. 5, Fig. 4 *c*), although the nucleus of an old megaloblast may be pyknotic, and when stained, appear very dark indeed. (See Pl. 4, Fig. 4 *e*.) Megaloblasts not infrequently show polychromatophilia. (See p. 784 and Pl. 4, Fig. 4 *c*, Pl. 5, Fig. 3, No. 26.) It is usually easy to differentiate well-marked normoblasts from megaloblasts, but many nucleated red blood-corpuscles are difficult to classify, and their classification depends to some extent upon the observer. (See Pl. 4, Fig. 4 *e*, and legend.) Most hematologists agree with Ehrlich that there is a distinct difference between normoblasts and megaloblasts, that the former represent the type of blood-formation in the adult, and the latter, the embryologic stage of blood-formation. The occurrence of transitional forms, however, is not thus precluded. It was formerly assumed that the fate of the nuclei in the two types varied, that the normoblasts became fully developed red blood-cells by extrusion of the nuclei, and the megaloblasts, by disintegration of the nuclei inside of the corpuscle. This opinion is, however, no longer held by modern hematologists. According to Nägeli, the destruction of the nuclei in the red cells by karyolysis (solution) and karyorrhexis (disintegration) must be considered physiologic (occurring in the bone-marrow); while the extrusion of normoblast nuclei into the plasma, which has been observed as well as inferred from the presence of free nuclei, is pathologic, if not artificial, because it takes place in the blood itself. Of clinical significance is the fact that normoblasts are observed in those anemic conditions in which the erythrocytes develop after the normal type of the adult organism. To this group belong cases of acute and chronic hemorrhages, and anemia following inanition, cachexia, blood-poisoning, hemoglobinemia, etc., *i. e.*, in so-called secondary anemias and also in chlorosis. Normoblasts have also been found in the blood in tumors of the bone-marrow. Megaloblasts, on the contrary, seem to be the clinical indication of some severe degenerative change of the bone-marrow, which it is presumed is subjected to abnormal chemical (toxic)influences. They are frequently found in pernicious anemia. This occurrence makes the prognosis grave and unfavorable, except in the type of anemia which is due to the presence of the Bothriocephalus. In leukemia both normoblasts and megaloblasts are observed, the latter predominating.

C. S. Engel[1] has noted the transitory appearance of megaloblasts not infrequently in the blood of children, although no serious significance need be attached to the finding.

In secondary anemia large numbers of normoblasts may at times be found in the blood –the so-called "blood-crises" of v. Noorden. Megaloblastic blood-crises have not been observed.

In poikilocytosis, deformed blood-corpuscles with nuclei are sometimes found. (See Pl. 4, Fig. 4 *d*.) They are termed poikiloblasts, and according to their morphology may be normoblasts or megaloblasts. The poikiloblast pictured in Pl. 4, Fig. 4 *d*, belongs to the latter type.

Cabot's Ring-bodies in Anemic Blood.—Cabot, and later Schleip, have, independently of each other, demonstrated peculiar ring-shaped or loop-shaped structures inside the red cells, which, according to Schleip, represent nuclear remains. They are present in anemic blood, especially in pernicious and severe secondary anemia, leukemia and pseudoleukemia, and in lead-poisoning. They are very oddly shaped, and stain best with Giemsa's or Leishman's stain, which colors them red or violet. They occur in red cells which appear normal in other respects, as

[1] Deut. med. Woch., 1906, vol. xxix, p. 1165.

well as in association with polychromatophilia and basophilic degeneration, and sometimes together with other nuclear remains. They are pictured on Pl. 5, Figs. 30–35, after Schleip's drawings. These peculiar structures are apparently products of a regressive metamorphosis of erythrocyte nuclei, and, like nucleated red cells and basophilic degeneration, seem to have some connection with pathologic phenomena of blood regeneration, to which, indeed, the latter also give evidence.

VARIETIES OF LEUKOCYTES

The following varieties of white blood-corpuscles may be differentiated (Ehrlich and Lazarus):[1]

I. LEUKOCYTES IN NORMAL BLOOD

(*a*) **Lymphocytes.**—These are derived from the lymph-glands, from other lymphadenoid tissues, and, according to more recent ideas, partly from the bone-marrow. They are, for the most part, small cells, usually about the size of red blood-corpuscles, often rather larger, with a large, centrally placed nucleus and a small margin of protoplasm. (See Pl. 4, Fig. 4, *h–l*, Pl. 5, Fig. 2, Nos. 10–13, and Pl. 6, Fig. 1, No. 7.) The nucleus stains rather intensely with nuclear stains, especially hematoxylin, somewhat less intensely with methylene-blue, and faintly with the triple stain. Between nucleus and protoplasm we can frequently see a narrow zone, either very faintly stained or without color. Ehrlich and Lazarus believe it to be due to an artificial retraction. In children especially and also in adults large lymphocytes are found as well as these small ones. These may be double the size of red blood-corpuscles, but are otherwise very much like the smaller ones in appearance (Pl. 4, Fig. 4, *n* and *m*, and Pl. 5, Fig. 2, Nos. 10 and 12).

They must not be confused with true so-called large lymphocytes or, better, lymphoid cells (p. 793, Pl. 4, Fig. 3, *c*, and Pl. 5, Fig. 3, Nos. 22 and 23), which are pathologic. The nuclei of the lymphocytes possess a coarse chromatin reticulum, and, after fixation at high temperatures, show one or two (never more) nucleoli, which have at times a deeply stained nucleolar membrane (Pl. 5, Fig. 2, No. 10). These nucleoli are most clearly recognized in smears stained with methylene-blue after fixation at high temperature, but are not detected in the ordinary Jenner and triacid preparations. In the protoplasm a basophilic reticulum can be demonstrated by staining with methylene-blue. This is best developed at the periphery, and is scanty near the nucleus (Pl. 4, Fig. 4, *i* and *m*, Pl. 5, Fig. 2, No. 2, and Pl. 6, Fig. 2, No. 7). Lymphocytes show no granulations with ordinary stains, but by using the azure dyes (Giemsa and Leishman stains), the so-called azure granules, of a red or violet tint, may be found in a minority of the cells (in one-third, according to Nägeli, Pl. 5, Fig. 2, No. 10). The nature and significance of these granules are not clear. They are usually considered products of the senile degeneration of the lymphocytes, and not true granulations, like those of other leukocytes. In lymphatic leukemia they are usually absent, but the author has found them even here.

In triacid preparations the nuclei of the lymphocytes appear pale bluish green, the protoplasm almost colorless or a pale pink (Pl. 6, Fig. 1, No. 7). Methylene-blue stains the nucleus more deeply or more faintly than the cell-body, depending on the degree of fixation. Pyronin

[1] Ehrlich and Lazarus, Anemia, in Nothnagel's System.

DESCRIPTION OF PLATE 4.

FIG. 1.—Pernicious Anemia: *a*, Normal erythrocytes; *b*, erythrocytes poor in hemoglobin; *c*, poikilocytes; *c'*, microcytes; *d*, macrocytes; *e*, polychromatophil erythrocytes; *f*, basophil erythrocytes; *g*, polychromatophil megaloblast; *h*, polynuclear neutrophil leukocyte. (Magnified 570; oil-immersion Leitz $\frac{1}{12}$, oc. 1; tube-length 170 mm. Jenner's stain).

FIG. 2.—Myelemia: *a*, Erythrocytes; *b*, polynuclear neutrophil leukocytes; *c*, neutrophil myelocytes with large nuclei; *d*, neutrophil myelocytes with small nuclei; *e*, polynuclear eosinophil leukocyte; *f*, eosinophil myelocytes; *g*, mast-cell. (Magnification and stain as in Fig. 1.)

FIG. 3.—Simple Elements of the Blood: *a*, Basophilic erythrocyte; *b–g*, various forms of erythrocytes; *b*, normoblast; *c*, polychromatophil megaloblast; *d*, poikilomegaloblast; *e*, polychromatophil erythroblast the size of which corresponds with the megaloblasts, but the nucleus of which is of the normoblast type; *f*, punctate megaloblast; *g*, megaloblast with nucleus split into four parts; *h–l*, various forms of small normal lymphocytes from the same preparation; *k*, the most common form; *m* and *n* (see also Fig. 4 x), large normal lymphocytes (in the common form): these all stain more deeply than the pathologic lymphocytes shown in Fig. 4; *o*, large mononuclear leukocyte from normal blood; *p*, form intermediary between the mononuclear and polynuclear leukocyte containing sparse granules. (Magnification and staining as in Fig. 1.)

FIG. 4.—Acute Lymphoid Leukemia: *a*, Erythrocytes; *b*, polynuclear neutrophil leukocytes; *c*, large lymphocytes; *d*, neutrophil myelocyte; *e*, polychromatophil erythroblast; *f*, free nuclei of normoblast. (Magnification and staining as in Fig. 1.)

PLATE 4.

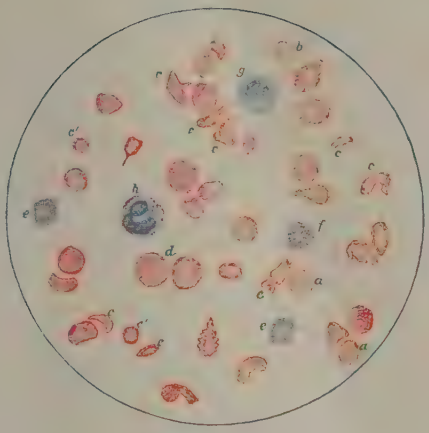


FIG. 1.

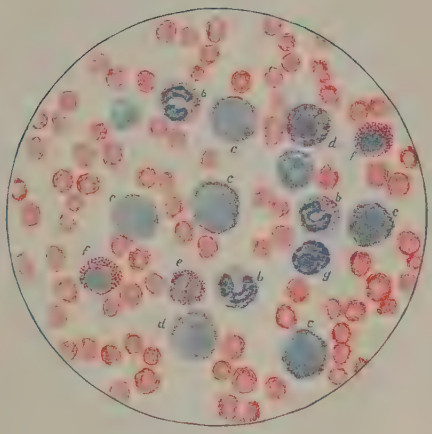


FIG. 2.

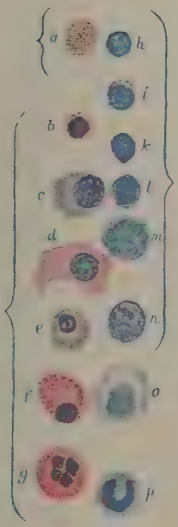


FIG. 3.

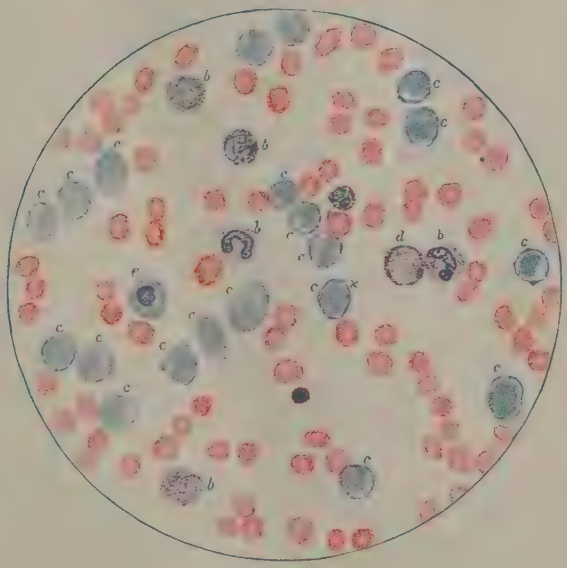


FIG. 4.

methyl-green stains the cell-body an intense red, the nucleus blue, and the nucleolus pink. Azure (Giemsa's and Leishman's stains) colors the protoplasm blue and the nucleus a deep violet.

Lymphocytes are fragile structures, and even slight pressure suffices to tear the protoplasm away either wholly or in part from the periphery, so that the cells assume a ragged contour (Pl. 4, Fig. 3, and Pl. 5, Fig. 2, No. 11).

They exhibit very slight active movements on the warm stage, and their migration from the blood-vessels cannot be regarded as proved. Lymphocytes contain neither autolytic ferments nor oxydases. They do not react to the guaiac test (lymphatic leukemia, see p. 856).

The normal number of lymphocytes is 22 to 25 per cent. of the total number of leukocytes, *i. e.*, 1500 to 1700 per cubic millimeter (up to 70 per cent. in children, according to Nägeli). During digestion the number of lymphocytes should probably increase *digestion lymphocytosis*.

According to Ehrlich and Pappenheim,[1] lymphocytes are also found in the bone-marrow; in fact, the latter believes that these lymphocytes of the bone-marrow are the progenitors of all the myeloid elements. Nägeli considers Pappenheim's belief to be erroneous. According to him, the lymphocytes are developed chiefly in the lymph-nodes, in the follicles of the spleen, and perhaps also in the small disseminated accumulations of lymphoid tissue in different organs, *e. g.*, the intestine. Nägeli calls the lymphocyte-resembling cells in the bone-marrow "myeloblasts," and, as opposed to other authorities, considers that lymphatic structures have not been demonstrated in the bone-marrow. (See p. 793.)

(*b*) **Large Mononuclear Leukocytes** (Pl. 4, Fig. 4, *o*, and Pl. 5, Fig. 2, Nos. 7–9, and Pl. 6, Fig. 1, Nos. 5 and 6).—These are cells two or three times as large as red blood-corpuscles, 12 to 20 μ in diameter, with large oval nuclei usually situated eccentrically and staining faintly (less intensely than the nuclei of lymphocytes). They are easily damaged in making the smears, and then exhibit irregular outlines. There is a little less distinct reticulum in the protoplasm than in that of the large lymphocytes, with which these cells are often confused. Granules are rarely seen when they are stained with methylene-blue, but though they were formerly considered free from granules, there are, according to Nägeli, in many specimens, at least in pathologic cases, scanty, fine neutrophile granules which may be demonstrated by using a good triacid stain. There is thus no distinct boundary between large mononuclears and transitionals. With Giemsa's and Leishman's stains azure granules may be demonstrated, and, according to Nägeli, the former imparts a dusky tint to the protoplasm, though not in all specimens. The position of large mononuclears in the classification of leukocytes is still very uncertain. Ehrlich's school regards them as quite immature elements of the bone-marrow at an earlier stage of development than the myelocytes. Pappenheim thinks they belong to the lymphocytes, while Nägeli considers them especially differentiated, mature elements of the myeloid group. They are frequently mistaken for large lymphocytes, but have more protoplasm and a nucleus which stains rather faintly. Their differentiation is sometimes, however, very difficult. It is perhaps easiest in pyronin methyl-green preparations, in which the cell-bodies of the lymphocytes are an intense red, and those of the mono-

[1] Neuere Streitfragen aus dem Gebeite der Hämatologie, Zeit. f. klin. Med., 1902, vol. xlvii, pp. 3 and 4.

nuclears a pale rose color. This stain, however, is not suitable for ordinary examinations, so that the author recommends the use of Jenner's solution after fixation at high temperature. In such preparations the lymphocytes are easily recognized, since in contrast to the large mononuclears their cell-bodies are darker blue than the nuclei. The normal percentage of this group is about 1 per cent. of the leukocytes, *i. e.*, 70 for each cubic millimeter.

(*c*) **Transitional Cells** (Pl. 4, Fig. 4, *p*, Pl. 5, Fig. 2, Nos. 5 and 6, and Pl. 6, Fig. 1, No. 4).—These are very much like (*b*), except that the nucleus is quite irregular in shape and stains more deeply and the protoplasm exhibits a less distinct reticulum and contains a few fine neutrophilic granules. They are regarded as derivatives of the marrow and ancestors of group (*d*). They occupy a position between the exclusively pathologic myelocytes and the polynuclears, and are actually immature forms of the latter. The number of transitional cells is normally from 2 to 4 per cent. of the leukocytes, *i. e.*, 140 to 280 per cubic millimeter. In counting they are usually included in one group with the related type (*b*). The normal number for the combined group (*b* and *c*) is about 3 to 5 per cent., *i. e.*, 210 to 350 per cubic millimeter.

(*d*) **Polynuclear** or, better, **polymorphonuclear neutrophilic leukocytes** (Pl. 4, Fig. 1, *h*, 2 *b*, 3 *b*, Pl. 5, Fig. 2, No. 1, and Pl. 6, Fig. 1, No. 1), are from 9 to 12 μ in size; they are characterized by a polymorphous, irregularly shaped or bent nucleus, which occupies only a small part of the cell, and which may be readily confounded with multiple nuclei. Indeed, acted upon by acetic acid, it may be separated into several nuclei, a change which also occurs probably when the leukocytes leave the vascular system and become pus-corpuscles (hence the incorrect name "polynuclear cells," which is almost impossible to eradicate). The nuclei stain very intensely, the chromatin is arranged in loops, the protoplasm is very densely packed with neutrophilic granules, and elsewhere oxyphilic; but in the young cells there is a faintly neutrophilic reticulum. No nucleoli are visible. Ehrlich's triacid solution stains the characteristic granulations most distinctly, imparting to them a violet color (Pl. 6, Fig. 1, No. 1). They are stained the same tint, but less surely, and more as a result of accident, by Jenner's (Pl. 4, Fig. 1, *h*, Fig. 2, *b*, and Fig. 3, *b*) and Giemsa's (Pl. 4, Fig. 2, No. 1) solutions. After decided fixation the eosin of these two stains imparts a deeper red tint to the neutrophile granulations. They may then be differentiated from coarser eosinophile granulations by their delicacy. The polynuclear neutrophiles arise exclusively from the bone-marrow, and in fresh preparations exhibit active ameboid movement. As true phagocytes, and by virtue of their fermentative properties (they contain oxydase and tryptic ferments), they play an important physiologic rôle. They are the essential constituents of pus, where, however, they lose many of their characteristics, especially, to a greater or less degree, the distinctive staining of their neutrophile granules and of their nuclei. The pathologic iodin reaction affects chiefly these cells. (See p. 781.) The normal number of polymorphonuclear cells is about 70 to 72 per cent. of the leukocytes, *i. e.*, 4900 to 5040 per cubic millimeter.

(*e*) **Eosinophilic Cells** (Pl. 4, Fig. 4, Fig. 2, *e*, Pl. 5, Fig. 2, No. 2, and Pl. 6, Fig. 1, No. 2).—These resemble the polymorphonuclear

PLATE 5.

Fig. 1

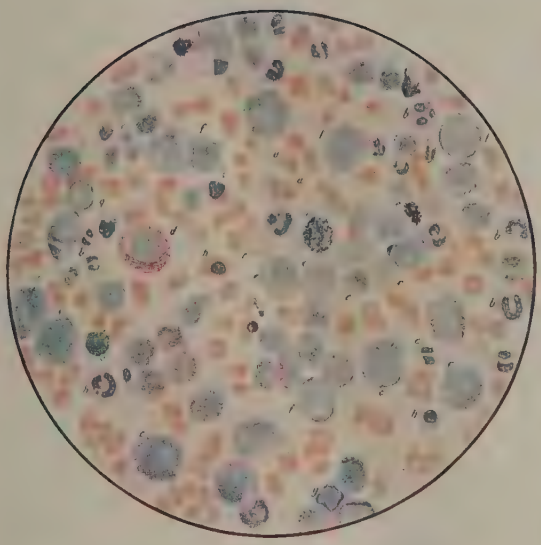


Fig. 2.

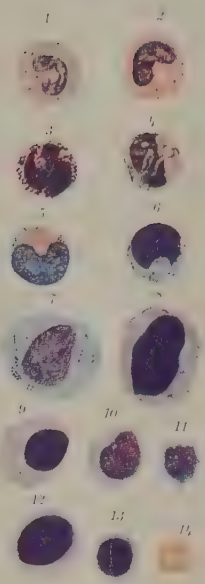


Fig. 3.

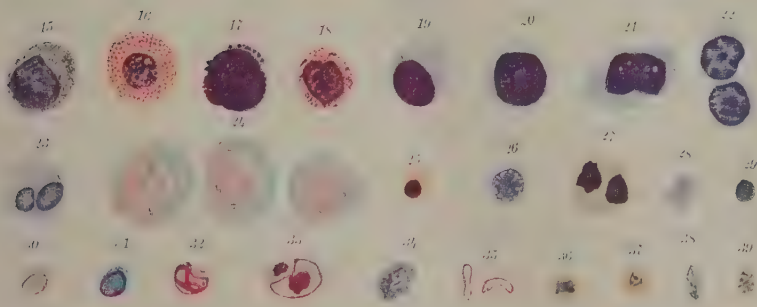


FIG. 1.—A case of myeloid leukemia. (Enlarged, 570×; oil-immersion, $\frac{1}{12}$.) Jenner stain: *a*, Erythrocytes; *b*, neutrophile polynuclear leukocytes, some of them dwarf; *c*, neutrophile myelocytes, some of them dwarf; *d*, eosinophile myelocyte; *e*, mast-cells and mast-cell myelocytes; *f*, myeloblasts; *g*, lymphocytes; *f*, normoblasts.

FIG. 2.—Normal blood-corpuscles. (Oil-immersion, $\frac{1}{12}$; enlarged about 700.) Giemsa's stain: 1, Polynuclear neutrophile leukocyte; 2, polynuclear eosinophile leukocyte; 3, polynuclear mast-cell, some of the granules stained, some unstained; 4, mast-cell, with most of the granules unstained; 5, transition cell with violet protoplasm; 6, transition cell with blue plasm; 7, 8, 9, various forms of mononuclear cells; 10, 11, 12, 13, various normal lymphocytes; 14, erythrocytes.

FIG. 3.—Pathologic blood-cells. Giemsa's stain (same magnification): 15, Neutrophile myelocyte; 16, eosinophile myelocyte; 17, mast-cell, with deeply staining granules; 18, pathologic myeloid cell with both basophile and eosinophile granules; 19, 20, 21, Türk's irritation forms (so-called plasma cells); 22, pathologic lymphocytes (Rieder's forms), with indented nuclei; 23, pathologic lymphocytes with double nucleus; 24, myeloblast (after Nägeli); 25, normoblast; 26, polychromatophile megaloblast; 27, granular erythroblast with two nuclei; 28, polychromatophile erythrocyte; 29, free nucleus of a normoblast; 30–35, several Cabot-Schleip ring-forms (after Schleip); 36–39, malarial plasmodia; 36, usual form; 37, ring-form; 38, crescent; 39, mulberry body.

neutrophiles, except that the small neutrophilic granules are replaced by coarse oxyphilic granules. The triacid mixture stains the latter a red to an orange or a copper color. Jenner's and Giemsa's stains produce a pure eosin color. The coarse granules refract the light so strongly that these cells are readily recognized without staining. When unstained, however, they might be mistaken for mast-cells (see below), although the granules of the latter are usually much coarser. The eosinophiles normally furnish between 2 to 4 per cent. of the leukocytes, *i. e.*, 140 to 280 per cubic millimeter.

Eosinophilia (an increase in eosinophiles) is present in most cases of myelogenous leukemia, at the height of scarlet fever, in all forms of helminthiasis, in asthma, hay-fever, and many cases of emphysema, and in many skin diseases—pemphigus, urticaria, prurigo, eczema, and mercury dermatitis. (See p. 808.) Nägeli found eosinophilia frequently in neurasthenia and also in nervous diarrhea. It occurs during convalescence from most infectious diseases. On the other hand, the eosinophiles disappear in insufficiency of the bone-marrow, pernicious anemia, and at the height of all infectious diseases except scarlet fever. Eosinophiles are developed exclusively in the bone-marrow. The mononuclear eosinophiles present in the sputum of asthma and of the so-called eosinophile bronchitis are apparently degeneration forms of the polymorphonuclear eosinophiles of the blood.

(*f*) **Mast-cells** (Pl. 4, Fig. 2, *g*, Pl. 5, Fig. 2, Nos. 3 and 4, Pl. 6 Fig. 1, No. 3) are cells of the polymorphonuclear or transitional type, with marked basophilic granules, which are quite large, uneven, and irregularly distributed, and which usually are not much larger than the eosinophile granules. They are not distinctly stained by the triple stain, but are visible as little cavities in the protoplasm (negative staining, Pl. 6, Fig. 1, No. 3). They are, on the other hand, deeply stained with alcoholic methylene-blue or with Jenner's stain, and if the latter contain an azure dye, they are metachromatic, *i. e.*, violet instead of blue. Leishman's stain imparts a deep violet to black color to these basophilic granulations. Giemsa's solution stains only a part of them (Pl. 5, Fig. 2, Nos. 3 and 4). They arise exclusively from the bone-marrow. The number of these cells in normal blood is about 0.5 per cent. of the leukocytes, *i. e.*, 35 per cubic millimeter.

These figures for the proportions of the various kinds of leukocytes in the blood should be modified in the case of children below five years of age, where the mononuclear cells predominate. From the fifth year on, the polynuclear cells reach 50 per cent.[1] There is as yet no more accurate information regarding the occurrence of any individual type of leukocyte in children of different ages.

II. PATHOLOGIC LEUKOCYTES

(*a*) **Myelocytes.**—(*α*) **Neutrophilic Myelocytes** (*Mononuclear Neutrophiles; Marrow-cells; "Markzellen"* (Ehrlich), *improperly often designated as myelocytes without qualification*).—These cells are the immature progenitors of polynuclear neutrophiles, which normally remain in the bone-marrow. They are large cells with a large, faintly staining nucleus, differing from the large mononuclear cells of normal blood by the presence in the protoplasm of a much more profuse content of

[1] Besredka, Ann. Pasteur, 1898, No. 5, p. 327 et seq.

neutrophile granules, and by the diminished amount of the protoplasm (see Pl. 4, Fig. 2, *c* and *d*, Pl. 5, Fig. 1, *c*, Fig. 3, No. 15, and Pl. 6, Fig. 2, No. 9—mononuclear cells). They form the distinctive characteristic of the blood in *myelogenous leukemia;* but they may be found under other pathologic conditions; for instance, in *malignant tumors of the bone-marrow*, in *anæmia pseudoleukemica infantum* of v. Jaksch, and in leukocytoses. (See p. 804 et seq.) They are not found in normal blood, or if so, they are so scattered that they are not included among normal leukocytes. There is, as in most immature myeloid cells, a faint basophile reticulum. The cells vary in size. The nucleus is usually faintly stained, but may assume a deeper tint. Myelocytes play approximately the same rôle in the life of white blood-cells that erythroblasts do in the life of red cells.

(β) **Eosinophilic Myelocytes** (*Mononuclear Eosinophiles*, see Pl. 4, Fig. 2, *f*, Pl. 5, Fig. 3, No. 16, and Pl. 6, Fig. 2, No. 10).—Ehrlich and Lazarus consider them to be progenitors of normal eosinophilic cells, bearing the same relation to these cells as do the neutrophilic myelocytes to the neutrophilic polymorphonuclears. They occur, like the latter, especially in myelogenic leukemia. Very small cells of this type, which are not infrequently observed in leukemia, have been termed eosinophilic dwarf-cells.

(γ) **Basophile myelocytes** (*marrow mast-cell myelocytes*), analogous to the basophile leukocytes, resemble the other myelocytes (α and β) except that they show basophile granulations. They are, as a rule, small.

The presence of great numbers of all types of myelocytes in the blood (usually the neutrophile myelocyte, α) always points to a serious change in the bone-marrow. According to Ehrlich, their occurrence during leukocytosis indicates that immature elements have reached the blood from the bone-marrow through the influence of chemotaxis. It depends also in some measure on the insufficiency of the bone-marrow. The appearance of many such cells at the height of an infection (*e. g.*, in pneumonia and diphtheria) is of bad prognosis. (See pp. 800 and 805.) The presence of myelocytes is of great diagnostic importance in the metastases of malignant tumors in the bone-marrow.

(*b*) **Small Neutrophilic Pseudolymphocytes** (*Neutrophil Dwarf Leukocytes;* see Pl. 6, Fig. 3, *b*).—These are small mononuclear cells with a deeply staining nucleus and neutrophilic granules. They are very rare. The presence of the deeply stained nucleus differentiates them from the small myelocytes. Ehrlich and Lazarus believe that they result from the division of ordinary polynuclear cells.

(*c*) **Irritation forms** (Türk), recently called "*plasma cells*" (see Pl. 5, Fig. 3, Nos. 19, 20), are mononuclear cells which resemble the lymphocytes in their characteristics, but are sometimes larger and without granules. They contain a relatively large amount of protoplasm, so that the nucleus seems smaller than those of lymphocytes. It is round or oval, and frequently placed eccentrically. It is colored a dusky grayish brown by the triacid stain (according to Nägeli), and the protoplasm a deep reddish brown. Methylene-blue brings out the reticulated structure in the protoplasm, which is strongly basophile. Giemsa's and Leishman's solutions produce the same effect. The latter dye stains the nucleus a moderately deep violet, and the protoplasm a deep blue (Pl. 5, Fig. 3, Nos. 19–21).

PLATE 6.

Fig. 1.

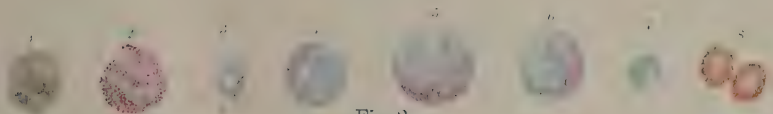


Fig. 2.

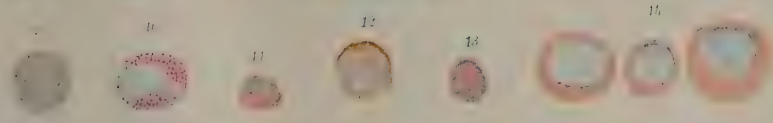


Fig. 3.

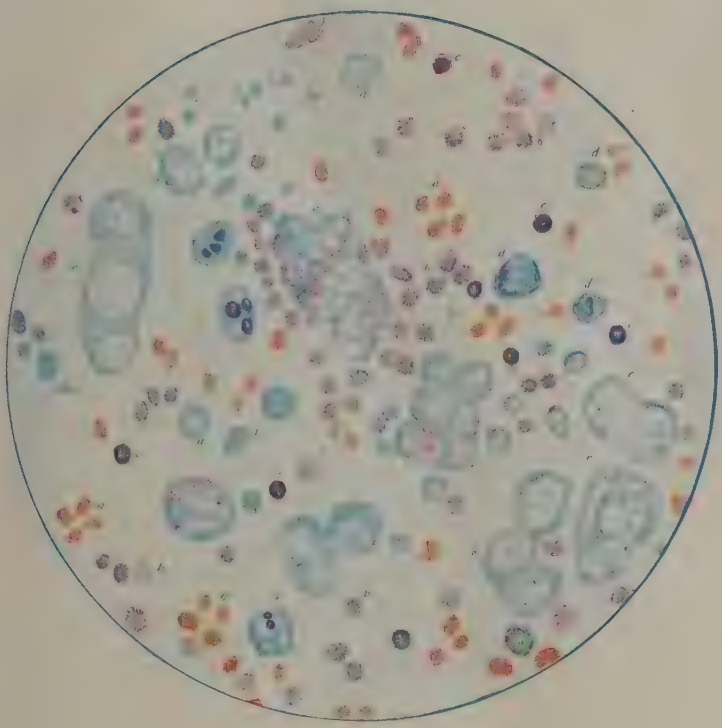


FIG. 1.—Normal blood-corpuscles (triacid stain); ×700: 1, Polynuclear neutrophile leukocyte; 2, polynuclear eosinophile leukocyte; 3, neutrophilic myelocyte; 4, transitional cell; 5 and 6, large mononuclear leukocyte; 7, lymphocyte; 8, erythrocyte.

FIG. 2.—Pathologic blood-corpuscles (triacid stain); ×700: 9, Neutrophile myelocyte; 10, eosinophile myelocyte; 11, normoblast; 12, megaloblast; 13, polychromatophilic erythrocyte; 14, three myeloblasts (after Nägeli).

FIG. 3.—Exudate from tuberculous pleurisy (Jenner's stain): *a*, Erythrocytes; *b*, neutrophile dwarf leukocytes; *c*, lymphocytes; *d*, endothelial cells of the pleura; *e*, endothelial masses, with neutrophile leukocytes enclosed or attached; *f*, endothelial cell containing a binuclear normoblast.

With pyronin methyl-green the cell-body appears a beautiful red, the nucleus a dusky grayish blue to violet, in contrast to the pale-blue nuclei of the lymphocytes. The nuclei often show mitotic figures. These cells are found in certain (lymphatic) leukemias and, according to Nägeli, even in leukocytosis and severe anemia. Türk found them under the same conditions with the myelocytes as a product of the irritation of the bone-marrow, hence the name, *irritation forms*. Nägeli formerly regarded them as myeloid forms without granulations and as only pathologic; while Schleip considers them descendants of the lymphocytes, an opinion in which Nägeli seems recently to have concurred, at least so far as their appearance in leukemia is concerned.

(*d*) **Pathologic Large Lymphoid Cells.**—In this class belong, first of all, the lymphocytes of leukemic and pseudoleukemic blood, which, on account of their size, are often called briefly large lymphocytes, a name not quite suitable, since there are also small types and since even the large forms are essentially different from the normal large lymphocytes mentioned on p. 788. It is perhaps more fitting, in order to clear up this confusion, to call them large pathologic lymphoid cells. (See Pl. 4, Fig. 3.) They have the general characteristics of normal lymphocytes, but differ from the latter in their size, which is frequently twice as great, and their defective staining qualities, which may be demonstrated with the triacid as well as with Jenner's solution. This is true of the nucleus as well as of the cell-body. They stain better by Giemsa's, Leishman's, and the eosin-hematoxylin methods. But even then the protoplasm is pale and the nucleus poor in chromatin. One or two nucleoli are present in the latter. The nuclei often show peculiar changes (indentations and fractures), described by Rieder[1] and by Ehrlich and Lazarus.[2] (See Pl. 5, Fig. 3, Nos. 22 and 23 and Schleip's[3] excellent plates.) The practiced observer will not confuse these forms with the broken nuclei of the polynuclear cells. Azure granules are seen only very rarely in these lymphoid cells.

Nägeli considers these pathologic, usually large, lymphoid cells the ancestors of ordinary lymphocytes, and assumes that they are formed in the germinal centers of the lymph-nodes and in the follicles of the spleen, since they correspond to the cells in those places. They appear in the blood in all cases of lymphatic leukemia, especially in the acute forms, and, furthermore, in lymphomatosis and lymphocytosis, *e. g.*, in typhoid fever (Nägeli).

Besides these pathologic large lymphocytes, there occur, in analogous conditions, smaller cells (the size of the ordinary lymphocytes) which differ from the latter chiefly in their paucity of chromatin.

(*e*) **Myeloblasts** (Nägeli).—By this term Nägeli designates marrow-cells without granulations, which reach the blood-stream in severe diseases of the bone-marrow and are the ancestors of the myelocytes. Formerly, and to some extent even now, they were classed by many writers as lymphocytes. They are found especially in myeloid leukemia, a strong argument in favor of their myeloid character. Nägeli has shown that they differ from large pathologic lymphoid cells (*d*), with which they were until now confused, principally by the capacity of their nuclei to take up the triacid stain. In contrast to the pale nuclei of the cells of group

[1] Rieder, Atlas der klin. Hämatologie, 1893.
[2] The Anemias in Nothnagel's System, 1905.
[3] Schleip, Atlas der Blutkrankheiten, Urban und Schwarzenberg, 1907, Fig. 47.

(*d*) the nuclei of myeloblasts become a dusky grayish blue, while the protoplasm appears rose colored (Pl. 6, Fig. 2, No. 14). With methylene-blue, and also with Giemsa's and Leishman's stains, the protoplasm is seen to be rather decidedly basophilic (Pl. 5, Fig. 3, No. 24). Even in myeloblasts stained with methylene-blue after strong fixation by heat the nuclei are paler than the protoplasm, and the nucleoli, in contrast to those of lymphocytes, are barely visible and number 2 to 4 (usually 3 or 4). One can best convince himself of the numerous nucleoli by the use of Giemsa's stain, which colors them a distinct blue, distinguishing them from the pink nucleus (Pl. 5, Fig. 3, No. 24). With pyronin methyl-green the nucleoli appear to be pale pink or almost colorless, round structures in a blue nucleus. In contradistinction to normal lymphocytes no azure granules are present. Nägeli considers that the presence, in myelogenous leukemia, of numerous intermediate forms, from myeloblasts to cells with neutrophile granulations, particularly favors the supposition that these structures belong to the myeloid system. The author confirms this finding and its occurrence also in the bone-marrow. Nägeli lays down the following rules for the differentiation of myeloblasts from other cells.

"Myeloblasts differ—(1) from large mononuclears by their round or oval nucleus, rich in chromatin; (2) from pathologic large lymphoid cells by the better staining nucleus, richer in chromatin, and containing more nucleoli, which are not clearly stained by methylene-blue; (3) from older, larger, normal lymphocytes (such as are found in children, p. 788), by their darker nucleus, strongly basophilic protoplasm, and the absence of azure granulations."

According to Nägeli, myeloblasts are found in pernicious anemia and in the anemias of children, as well as in myeloid leukemia.

DIFFERENTIAL COUNTING OF LEUKOCYTES AND THEIR PROPORTIONS UNDER NORMAL CONDITIONS

If it be desired to differentiate simply the mononuclear and polynuclear elements, the differential count may be made in the ordinary counting chamber from blood treated with dilute acetic acid, which renders the nuclei quite distinct. For the further differentiation of the several varieties of leukocytes (see p. 776), dry specimens stained with eosin hematoxylin may be employed. These preparations, however, suffice to establish merely the gross relations, *e. g.*, to differentiate and form a judgment of the severity of lymphatic and myeloid leukemia or to recognize eosinophilia. For examination and a complete differential count of all the varieties of the white cells we must employ other methods, *e. g.*, Ehrlich's triacid mixture, Jenner's, Giemsa's, or Leishman's solutions. (See p. 777 et seq.) If the white cells be only moderate in number, the visual field of the microscope may be employed as the unit of space for their enumeration. By tabulating the numbers of each variety of leukocytes seen in a large number of fields it is easy to calculate their relative percentage. With the help of a movable stage the entire preparation may be counted exactly. If, however, the number of white cells be materially increased, this process is very tedious. Ehrlich, therefore, devised and had Leitz manufacture a peculiar ocular, fitted with a simple removable screen, by means of which quadrilateral fields of any size desired may be secured. The size of the fields is selected to conform to the number of the corpuscles in the preparation. With this help both the total count and the differential

count of the different varieties of leukocytes can be very easily made; and sufficiently large absolute counts can be made by merely sliding the preparation to and fro. It is the most convenient and least tedious method of counting. Ehrlich employs it in determining the relative number of red and white cells; but for this purpose it is more convenient to compare the absolute numbers of red and white cells with each other, since otherwise their relative proportions possess neither physiologic nor diagnostic interest.

Whichever of the above-mentioned methods we may employ for the differential counting of the separate varieties of leukocytes, it is always advisable to control these relative counts by the absolute count of the leukocytes obtained in the usual way (see p. 757), and expressed in terms of the cubic millimeter of blood. This enables us to construct graphic curves,[1] which are very helpful in considering the changes in the blood-picture.

Our knowledge of leukocytosis was at first considerably restricted by the fact that attention was drawn exclusively to the determination of the quantitative relation between the white and the red corpuscles. Similarly, the limitation of the investigation to the determination of the quantitative relations of the various leukocytes, without due regard to the absolute number of these cells, has also considerably restricted our knowledge of this topic. The whole study of leukemia and pseudo-leukemia suffers from this practice, which still obtains, of expressing the results of the differential count as mere percentages. Our knowledge of these diseases will be advanced much further if we always estimate the absolute number of each type of cell per cubic millimeter, since, of course, an absolute increase or decrease of a particular kind of leukocyte warrants the conclusion of an irritative or depressive disturbance of function of the tissue in which it develops; while such a conclusion is impossible from the differential count alone.

DIRECT DIFFERENTIAL COUNTING OF STAINED BLOOD IN THE COUNTING-CHAMBER

Zollikofer's[2] *method* of staining fresh blood-preparations in the counting-chamber, and then determining the absolute number of the different kinds of leukocytes present, is a welcome simplification.

The two following solutions are required:

I

Eosin, w. g. (Grübler)	0.05
Formalin, conc. (40 per cent.)	1.00
Aquæ destillatæ	100.00
	Filter.

II

Methylene-blue, B. X. (Grübler)	0.05
Formalin, conc.	1.00
Aquæ destillatæ	100.00
	Filter.

Both solutions are kept in dark bottles, and before using are mixed in about equal quantities with a medicine-dropper.

The blood is drawn into a Thoma-Zeiss leukocyte counter, and diluted 20 times with the freshly mixed stain. The stain after being mixed must be used

[1] Die Leukocytose beim Typhus abdominalis, Deut. Arch. f. klin. Med., 1903, vol. lxvii.

[2] Zeit. f. mik. Technik, 1901.

immediately, because a precipitate is formed if it stand for any length of time. The dilution of the blood with the stain must be done very rapidly, for if the blood remain in the capillary tube for any length of time, the red blood-corpuscles become visible.

The pipet is shaken for about five minutes, and a drop then placed on the counting-slide. The red blood-corpuscles, unless nucleated, are invisible. The leukocytes are preserved, and the individual kinds can be distinguished. The α (eosinophile) granules are stained yellowish to carmin, and are characterized by their size. The ε (neutrophile) granules are grayish violet, often filling up the entire body of the leukocyte, but in rare cases scattered only in the protoplasm. The γ (basophile) granules remain unstained. The leukocytes without granulations may be distinguished by the relative amount of protoplasm and the size of the nucleus, as lymphocytes or large mononuclear cells. The nucleus is less distinctly stained in the granular types, and for this reason the mononuclear granulated leukocytes (myelocytes) cannot be accurately separated from the polynuclear. The blood-platelets are of a bluish-violet tinge, and may be recognized by their typical grape-like arrangement. The proportion of the eosin to the methylene-blue can be so regulated that neither the nuclei nor the granules predominate.

The same mixture can be used in dry preparations which have been well fixed at 120° C. They should be stained for from one-half to one minute. Besides differentiating the various kinds of leukocytes, it stains malarial parasites, bacteria, and the basophilic granules of the erythrocytes, and shows the polychromatophilic changes of the red-cell plasma.

W. Türk makes use of the following diluting fluids: glacial acetic acid, 3 cc.; aqua dest., 300 cc.; 1 per cent. aqueous gentian-violet solution, 2 to 3 cc.; and he claims that the clear nuclear staining resulting therefrom is in most cases sufficient to differentiate the leukocytes. The eosinophile cells, of course, cannot be recognized because their granules are dissolved. The mast-cells, since their granules run together, are stained a uniformly dark violet, and after some practice will not be confused with other structures. Only in myeloid leukemia are some of the mast-cells not sufficiently characteristic. Even normoblasts may be recognized in these preparations, and, less surely, megaloblasts. Polychromatophilia may be recognized in that the discoplasm, which is otherwise hardly visible, appears pale blue. Türk believes that the use of this fluid simplifies the differential count in cases where it is not necessary to determine details not recognizable in such a preparation.

LEUKOCYTOSIS AND LEUKOPENIA

By the term *leukocytosis* is understood the state of the blood, occurring under various conditions, in which there is an increase of the white corpuscles, except where such an increase is due to the specific or idiopathic disease of the blood, leukemia. Most leukocytoses are characterized, in contradistinction to leukemia, by an increase in the polynuclear neutrophiles, which are derived from the bone-marrow, so that the term leukocytosis, used without qualification, usually means the increase of this kind of cell.

An unusual form of leukocytosis, except when it is associated with leukemia, is characterized by an increase in the number of lymphocytes —the so-called *lymphocytosis*.

Leukopenia is the reverse of leukocytosis, *i. e.*, a diminution in the number of leukocytes.

Leukocytoses are either physiologic or pathologic. The polynuclear elements of pathologic leukocytoses are usually neutrophilic, so that a polynuclear neutrophilic leukocytosis is, as a rule, pathologic. There is, however, a pathologic eosinophilic polynuclear leukocytosis. These pathologic leukocytoses are explained by the presence of chemotactic substances in the blood-plasma, most of which exert a positive influence on the neutrophilic, and but little on the eosinophilic, cells. A leukocytosis in which the third kind of granular cells, the mast-cells, are increased is not as yet known. In leukemia, however, these cells are usually very much increased; and perhaps in this disease there is some

little positive chemotactic influence from the blood upon the mast-cells.

Immature forms from the bone-marrow, especially myelocytes (see p. 791), reach the blood in most polynuclear leukocytoses. If abundant, they are evidence of a certain functional insufficiency of the bone-marrow. (See p. 791.)

PHYSIOLOGIC LEUKOCYTOSES

To this group belong the leukocytosis of digestion, the leukocytosis after exertion and after a cold bath, the leukocytosis of pregnancy and that of the new-born.

The *leukocytosis of digestion* begins about one hour after a meal, and reaches its maximum (a 30 to 40 per cent. increase of the white cells) in about three to four hours (Rieder). It is most marked after food rich in proteids. Considering the comparatively slight digestion leukocytosis, any great degree of pathologic leukocytosis can be recognized even during digestion. According to Rieder, both mononuclear and polynuclear cells are increased so that their relative percentage is unchanged. The eosinophiles, on the contrary, are much diminished.

Very little definite information is as yet at hand regarding the *leukocytosis after exertion and cold baths.* It is not yet known whether there is an actual increase in the total number of leukocytes, or whether this is only a pseudoleukocytosis, *i. e.*, one produced by an accumulation of leukocytes in the skin vessels. The *leukocytosis of pregnancy* may amount to 50 or 80 per cent., is present only in the later months of pregnancy, and disappears rapidly after delivery. The relative percentages of all varieties including the eosinophiles remain normal (Rieder).

Leukocytosis of the New-born.—The white count is two or three times the normal during the first day of life. It then diminishes to normal, and increases again after the first week, remaining for several weeks at about 50 per cent. above the normal. Rieder found in this leukocytosis a preponderance of the mononuclears. (See Lymphocytes, p. 789.) He also found that the blood of the new-born contained a high percentage of eosinophiles and normoblasts, and exhibited a moderate poikilocytosis.

THE BLOOD IN THE INFECTIOUS DISEASES; INFECTIOUS LEUKOCYTOSIS AND LEUKOPENIA[1]

Most infections cause a leukocytosis (polynuclear neutrophilia) probably through the influence of the toxins excited by the disease and produced in the body. This is generally understood to be a defensive reaction of the bone-marrow. In only a few infectious diseases is there a leukopenia.

K. Ziegler[2] found that, following the recession of the polynuclear leukocytosis, there regularly occurs a secondary and usually a transitory and brief increase in the large mononuclears. The lymphocytes next begin to increase above normal, while the neutrophile curve sinks still lower, so that the greatest increase in the lymphocytes often occurs at the same time when the neutrophiles are least. Ziegler calls this time the crisis of blood regeneration. From this point on the white cells begin to approach the normal. Toward the end of the lymphocytosis Ziegler usually found an increase in eosinophiles and mast-cells.

[1] Chiefly compiled from Rieder, Beiträge zur Kenntnis der Leukocytose, Leipzig, Vogel, 1892; Türk, Klinische Untersuchungen über das Verhalten des Blutes bei acuten Infectionskrankheiten, Wien und Leipzig, 1898; O. Nägeli, Ueber die Typhusepidemie in Oberbipp, ein Beitrag zur Aetiologie und Hämatologie des Typhus abdominalis, Correspondenzbl. f. Schweizer Aerzte, 1899, No. 18; and ibid., Die Leukocyten beim Typhus abdominalis, Deut. Arch. f. klin. Med., 1900, vol. lxvii, p. 279; Schindler, Zeit. f. klin. Med., 1904, vol. liv; Arneth, Die neutrophilen weissen Blutkörperchen bei Infectionskrankheiten, Jena, Fischer, 1904; Nägeli, Blutkrankheiten und Blutdiagnostik, Leipzig, Veit, 1908; and Ziegler, Arch. f. klin. Med., 1908, vol. xciv.

[2] Arch. f. klin. Med., 1908, vol. xcii.

These observations evidently imply a general formula for the typical relations demonstrated by Nägeli in typhoid fever as well as a general conformity to law whose physiologic meaning is not yet fully clear.

Ziegler, however, emphasizes the extreme variations of detail in the blood changes in different infections and different individuals affected by the same disease, so that it is difficult or impossible to construct such characteristic curves as Nägeli has done in typhoid fever. (See p. 798 et seq.) The duration of the blood reaction is also very variable. Thus in most cases of pneumonia, erysipelas, and perityphlitis, and in some cases of diphtheria and scarlet fever, the blood-picture becomes normal in four to six weeks, while in others this occurs only after six to ten weeks.

Ziegler's observations should be classed with those of Schindler on the regularity of the occurrence of myelocytes in infectious diseases, and with Arneth's studies on the "neutrophile blood-picture." (See p. 805 et seq.)

Infectious Oligochromemia.—An interesting and noteworthy phenomenon to which Hayem in particular has called attention is the reduction of hemoglobin and the red-cell count in most infectious diseases. There are apparently several causes for this: (1) An increased destruction of the red cells because of their susceptibility to the toxins and because of the increased metabolism in fever; (2) a toxic interference with their production; (3) a thinning of the blood through the febrile retention of water. The last is certainly not the only cause, since the red cell and the hemoglobin content would be equally affected by water retention, and, according to Nägeli, the hemoglobin quotient or color index is generally less than 1. The degree of oligochromemia generally varies with the severity of the infection. Whether its presence permits merely of judging the condition of the patient at a given time or whether it has prognostic value has not yet been decided. Irregular staining of the red cells, polychromatophilia, and basophilic degeneration as well as normoblasts and megaloblasts have also been demonstrated in the most varied infections. It would seem worth while to investigate these phenomena more closely by means of extended and systematic studies after the manner of the writers who have of late years paid almost exclusive attention to the study of the behavior of the white cells. For it is clear that outside of their physiologic importance in overcoming disease, the red cells, as well as the leukocytes, could furnish us with conclusions as to the condition of that powerful defensive organ, the bone-marrow.

THE BLOOD-PICTURE IN INDIVIDUAL INFECTIOUS DISEASES

Pneumonia

Pneumonia is usually accompanied by a pronounced leukocytosis. The degree does not correspond to the severity of the infection, nor does it permit of an absolute prognostic conclusion. The leukocytes, as a rule, run from 15,000 to 30,000 per cubic millimeter. A drop in their number usually begins on the day of the crisis, or sometimes on the day before. It is not, however, common to have the number drop below the normal after the crisis. The leukocytosis of pneumonia is composed of neutrophiles, the eosinophiles disappearing during the course of the disease. The reappearance of eosinophiles indicates that the height of infection has been passed, and is, therefore, suggestive of a favorable prognosis. It usually takes place on the day of the crisis, but sometimes one or two days before. Later the eosinophiles may be increased beyond the normal limits. A high normal leukocyte count with only a relative increase of the polynuclear neutrophiles indicates a severe infection and reduced resistance, although from it a bad prognosis should not be given. Leukopenia in pneumonia suggests a dubious prognosis, although it does not necessarily indicate a fatal termination.

Typhoid

In striking contrast to pneumonia typhoid is usually characterized by leukopenia. Nägeli, continuing Rieder's and Türk's investigations, studied the hematology of typhoid more minutely. He has arrived at the following conclusions:

In the first stage (ascending fever curve) there is probably a moderate neutrophile leukocytosis. This may be inferred from the condition found in relapses. It soon diminishes, and is then followed by a diminution in the neutrophiles. The eosinophiles disappear entirely or very nearly. The diminution of lymphocytes is moderate.

In the second stage (fastigium, continued fever) the number of neutrophiles and lymphocytes diminishes still further, although the latter may be somewhat increased toward the end of this period.

In the third stage (period of remissions) the lymphocytes are frequently increased, and sometimes decidedly so. The neutrophiles are still more diminished, and the eosinophiles begin to reappear at the end of this period. In adults the lymphocytes may remain few in number.

The fourth stage (descending fever curve) is characterized by a still further diminution of the neutrophiles, which reach their minimum during this period. The lymphocytes are considerably increased, and may be much more numerous than the neutrophiles (crossing of the two curves). The eosinophiles begin to increase slowly and regularly.

In the first days after the fever disappears the neutrophiles begin to increase. The lymphocytes are very abundant and the eosinophiles continue to increase. Some time after the disease has run its course there may be a considerable lymphocytosis, a marked increase of eosinophiles, and normal or slightly increased numbers of neutrophiles. This condition is most pronounced in young individuals, especially two or three months after defervescence. In adults it is less marked, and usually disappears within two months; but in children it persists considerably longer.

During the active stage of the disease the variations in the leukocytes are more pronounced in children than in adults, especially the lymphocytes. On the other hand, even if children are extremely ill, the number of leukocytes is rarely as low as in adults (apparently due to a less severe involvement of the bone-marrow and the lymphatic apparatus).

Non-typhoidal complications, of course, influence merely the number of neutrophiles. They are usually increased, but generally not excessively, by suppuration, cystitis, parotitis, pleuritis, bronchopneumonia, nephritis, etc. Absence of leukocytosis in spite of complications indicates an insufficiency in the function of the bone-marrow. This is a dangerous condition (impossibility of forming new neutrophiles).

The blood-findings (lymphocytosis) may persist long after the disease has disappeared; they are very characteristic, and, as Nägeli has shown, may prove that a patient has ambulatory typhoid, although he is apparently well, often with even greater certainty than is possible with Widal's reaction, a fact which may be of considerable importance in determining the beginning of an epidemic of typhoid, and which was used by Nägeli in the epidemic at Oberlipp.

Diagnosis.—Nägeli emphasizes the following statement as a law: "A disease in which eosinophiles are present in one-half normal, normal, or increased numbers cannot be typhoid; and the appearance of even a few of these cells must incite caution in the diagnosis." The converse of this law he considers untrustworthy. A persistent leukocytosis also argues strongly against typhoid. In regard to the differential diagnosis, Nägeli insists that in other forms of *enteritis* leukocytosis almost always occurs; in *tuberculous meningitis* there is no leukopenia; in *general miliary tuberculosis* leukopenia is absent in the early stages and seldom occurs at all; and in *chronic tuberculosis* the eosinophiles are either normal or increased in numbers. *Paratyphoid* behaves, according to Nägeli, the same as ordinary typhoid.

Prognosis.—Nägeli considers favorable—(1) A slight degree of leukopenia; (2) an incomplete disappearance of eosinophiles at the height of the disease; and (3) an increase in eosinophiles and lymphocytes in the third stage, indicating that the organism has begun to conquer the infection. In the presence of complications a marked leukopenia or even the absence of leukocytosis is of unfavorable import. Nägeli found that the blood-picture is not essentially altered after the administration of drugs or during digestion.

The cause of this most characteristic and interesting behavior of the blood in typhoid fever is, according to Nägeli's and Studer's experimental investigations, the pernicious influence of the typhoid toxins on the bone-marrow.

To complete this typhoid blood-picture, the diminution of fibrin, a fact first demonstrated by Hayem, should be noted. (See p. 771.)

The enumeration of the platelets in typhoid blood, by the new methods which permit of their absolute identification (see p. 809 et seq., has not, to the author's knowledge, been attempted. Hayem[1] found, however, a diminution (to as low as

[1] Du Sang, etc., Paris, Masson, 1889.

60,000) in his so-called "hematoblasts," which doubtless nearly correspond to the platelets. The author strongly recommends estimating the number of blood platelets from fresh preparations, since, with a little practice, this may be done without actual counting. According to the experience in his clinic, the blood-picture in typhoid set forth above is quite as important in the diagnosis of doubtful cases as is the serum reaction, especially when the latter is negative.

Typhus Fever

According to the few observations extant,[1] typhus fever is apparently accompanied by a neutrophile leukocytosis.

Acute Articular Rheumatism

In uncomplicated cases of this disease there is usually a slight polynuclear neutrophilic leukocytosis (rarely above 15,000), which persists so long as there is fever and exudation (Cabot and Türk). The leukocytosis increases if complications occur (pleuritis, pericarditis). Eosinophiles are absent only in the very early cases, before there has been any amelioration of the symptoms. Later, usually before the termination of the illness, they reappear. The presence of eosinophiles is of favorable prognostic importance in this disease also.

Diphtheria

Neutrophile leukocytosis is usually present in this disease. The eosinophiles seldom disappear completely. According to K. Ziegler, lymphocytosis and an increase in the eosinophiles follow the recession of the leukocytosis. In a particularly severe fatal case Schindler observed the presence of numerous myelocytes (see p. 805), and he is inclined to confirm C. S. Engel's statement that the presence of large numbers of these cells is of bad prognosis.

Meningitis

In epidemic cerebrospinal meningitis there is always a pronounced polynuclear neutrophilic leukocytosis of varying degree, usually with a diminution in, sometimes with disappearance of, eosinophiles; but the latter increase in numbers with temporary or permanent improvement. According to the experience in the author's clinic, the behavior of these cells is quite as suggestive as in typhoid fever. In tuberculous meningitis the leukocyte count may be normal or distinctly increased (up to 20,000 and more). Absence of leukocytosis, then, points toward tuberculous meningitis, but its presence does not exclude this disease.

Septicemia and Malignant Endocarditis

In this disease there is usually a considerable polynuclear neutrophilic leukocytosis, with diminution in the lymphocytes and eosinophiles. Sometimes myelocytes and normoblasts are found. The platelets are usually increased. Only the most severe cases are unaccompanied by leukocytosis or even exhibit leukopenia. Türk emphasizes the presence of normoblasts in sepsis as a factor in excluding typhoid, but, according to Nägeli, this is not decisive. The marked reduction in hemoglobin and the occurrence of hemolysis and hemoglobinuria, particularly in streptococcus septicemia, should be noted. (See p. 719 et seq.)

Erysipelas

In the majority of the cases there is a moderate degree of polynuclear neutrophilic leukocytosis; in the minority the leukocyte count may be normal or only slightly increased. The degree of leukocytosis is of no prognostic value, except that, when marked, it suggests the formation of pus [or pneumonia.—Ed.] The eosinophiles are diminished in number or absent at the height of this disease also.

Scarlet Fever

Here, too, there is an increase of polynuclear neutrophiles. The characteristic feature of the leukocytosis of this disease is its persistence, for it does not disap-

[1] Nägeli, Blutkrankheiten und Blutdiagnostik, Leipzig, Veit, 1908.

pear for several weeks after the rash and the fever have vanished, a fact which can be made use of for diagnosis after the disease has run its course. In the very beginning of the disease the lymphocytes are very much diminished. The eosinophiles are somewhat diminished as soon as the rash appears; but while it persists, and during the period of desquamation, they may be normal, or at times very decidedly increased. The persistence of leukocytosis after this disease has run its course may possibly have some prognostic value in regard to the danger of late nephritis. In mild cases it is also frequently associated, according to the author's experience, with the slight, often disregarded, rise in temperature of some tenths of a degree over 37° C. (98.6° F.), which persists for about a week, but is not a true relapse. This temperature rise is barely referred to in the literature. According to Neutra,[1] the iodin reaction of the leukocytes is constant in the first days of the disease, and especially marked in severe cases. Kotschetkoff found a pronounced eosinophilia in fatal cases, and Nägeli is of the opinion that it depends on the development of the rash and is absent in the absence of the latter.

Measles

According to Renaud and Lagriffoul, leukocytosis occurs only in the period of incubation and during the prodromal stage of measles, and disappears with the onset of manifest symptoms. In uncomplicated cases it is replaced by a leukopenia similar to that in typhoid. This is most noticeable during the period of eruption, and especially when the latter is at its height, and gradually recedes during desquamation. The ratio between the polynuclear cells and the lymphocytes remains undisturbed. After the rash has disappeared, the total number of leukocytes increases to the normal, and the actual number of large mononuclear cells may be above the normal. The eosinophiles in the beginning of the incubation period are increased in number (Renaud). With the onset of manifest symptoms, up to the height of the disease, they are either normal or diminished, but subsequently they become slightly increased. A subnormal or a persisting normal number of leukocytes may be useful in the differential diagnosis between measles and scarlet fever. A marked eosinophilia and leukocytosis would be in favor of scarlet fever as against measles.

Rubella

In contradistinction to measles there is in the incubation and prodromal periods of rubella a distinct hyperleukocytosis, which persists to a less marked degree during the eruptive stage (Lagriffoul, Soc. de biol., Oct. 13–27, 1906).

Small-pox (Variola and Varioloid)

In variola Brouardel found a leukocytosis which reached its maximum on about the sixth day. Recent researches have revealed the same condition even in the prodromal stage. It is marked during vesiculation and especially so during pustulation, when the white cells may number 40,000. Lymphocytes are few, but numerous, large, often exceptionally large, mononuclears are present. According to Courmont and Montagard, the latter may reach 40 to 50 per cent. of the white cells, so that throughout the disease a distinct "mononucleosis" is present, a fact of great weight in the diagnosis. Myelocytes and normoblasts, as well as Türk's irritation forms, may be numerous at the beginning of pustulation. The persistence of eosinophiles is noteworthy. Nägeli draws attention to the fact that even in normal children numerous mononuclear cells are present and, therefore, emphasizes the diagnostic importance of the occurrence of numerous myelocytes and normoblasts.

In the modified form of variola known as *varioloid* the findings are, on the whole, the same as in severe variola (Courmont and Montagard).

According to Courmont, the morphologic blood-examination is of very great importance, for it enabled him to reach a diagnosis in all doubtful cases even in the early stages.

Varicella

In this disease Erben found a normal percentage of eosinophiles and an increase of the mononuclear leukocytes in a normal white count.

Influenza

On account of the vague conceptions of this disease, the author desists from quoting the data in the literature on the blood-findings.

[1] Zeit. f. Heilk., 1906, No. 11.

Dengue Fever

According to Stitt,[1] the blood-picture in dengue is so characteristic that many cases in which the other clinical phenomena are not diagnostic may be recognized by the behavior of the blood. One finds a low percentage of polynuclears (40 per cent.), first a high (40 per cent.), then a low (10 per cent.), percentage of lymphocytes, and on the third or fourth day an increase of the large lymphocytes to 30 per cent., and of the large mononuclears to 40 per cent. Thus the curves of the small lymphocytes and the large mononuclears intersect. There are no data as to the absolute numbers.

Pertussis

Pertussis leads to an increase of the lymphocytes, and, to a less marked degree, also to an increase of the polynuclear leukocytes.

[Barach[2] found a typical blood-picture in this disease. At the onset there is a leukocytosis averaging 17,000 to 18,000, with increase of all the forms; then a small-cell lymphocytosis (51 per cent.) and a less marked increase in the number of large lymphocytes. Bilobed small lymphocytes and degenerated large mononuclears are frequently seen. Later there is a gradual decrease in the leukocytosis and a return to the normal differential count, except for a slight eosinophilia (5 per cent.), which may persist for months.—Ed.]

Mumps

In mumps, even with high fever, F. Pick[3] found no leukocytosis. He regards this of importance in the differential diagnosis of orchitis due to mumps from that due to gonorrhea, and concludes from it that the former is purely a serous inflammation. This, however, does not always seem to be the case, since other writers have found quite a high leukocytosis in mumps, as well as in mumps complicated by orchitis, evidently depending on the virulence of the disease.

Malta Fever

The few examinations extant in this disease reveal a normal number of leukocytes or a leukopenia.

Relapsing Fever

This disease gives rise to a marked neutrophile leukocytosis.

Tetanus

Very few data on the blood in tetanus exist. Apparently a moderate degree of leukocytosis occurs, but this is inconstant. (It may vary with the kind of infection.)

Rabies

Courmont and Lésieur found a neutrophile leukocytosis in this disease.

Anthrax

Anthrax causes a leukocytosis.

Cholera

The supposedly invariable concentration of the blood in this disease does not seem to be constant.[4] A high degree of leukocytosis (up to 60,000) may be present.[5]

Malaria

According to Türk, the ordinary benign cases of malaria regularly show a leukopenia both during the paroxysms and in the intervals. During the paroxysm the

[1] Philippine Journal of Sci., 1906, i, p. 513.
[2] Arch. Int. Med., July, 1908.
[3] Wien. klin. Rundschau, 1902, No. 16.
[4] Plehn, Deut. Arch. f. klin. Med., 1907, vol. xci.
[5] Biernack, Deut. med. Woch., 1895, p. 795, and Rogers, Lancet, 1902, p. 659.

percentage of neutrophiles is relatively increased at the expense of the lymphocytes and eosinophiles. Schindler has reached different conclusions. He observed a diminution of the leukocytes and an increase of the mononuclear cells between the paroxysms, with a reappearance of the normal figures at the height of the fever. Türk has counted the plasmodia as well as the leukocytes in this disease. (See p. 819.)

R. Poch[1] summarizes the results of his examinations of the blood in malaria as follows: At the beginning of a paroxysm of tertian or quartan fever there is occasionally an initial transitory polynuclear leukocytosis. With this exception leukocytosis is not observed in any stage of any form of malaria. Sometimes in tropical and often in tertian and quartan malaria the leukocytes are diminished in numbers during the height of the fever. Leukopenia throughout the course of the disease is not uncommon. In tertian and quartan fever all mononuclear cells are fewer during the hot stage. In all forms there is, with the fall in temperature, a relative increase in the large mononuclears which continues during the intervals and for some time during convalescence. An incompletely cured malaria may thus be detected. The eosinophiles are decreased in numbers during the paroxysm, but are usually normal at other times.

Thus it is evident that different writers disagree in regard to the findings, so that it must be assumed that quite complicated and irregular conditions obtain in this disease. However, one can in general designate as characteristic the persistent low polynuclear count, with a tendency to moderate increase in these cells at the onset of the paroxysm.

Another characteristic of malarial blood outside of the presence of the organisms is the usual occurrence of oligochromemia, often of high grade, which is caused by the direct destruction of the red cells by the parasites. In addition, all of those changes in blood morphology which are typical of the symptom-complex of so-called pernicious anemia frequently occur (megalocytosis, poikilocytosis, polychromatophilia, and basophilic degeneration of the red cells, megaloblasts, and myelocytes). The presence of pigment within the leukocytes (the large mononuclears and polynuclear neutrophiles) is of importance in the diagnosis. The presence of hemoglobin in the blood-serum, with or without hemoglobinuria (black-water fever), especially after the excessive use of quinin, is also noteworthy. [Most writers in America agree in considering an increase in the large mononuclear cells a characteristic of the blood-picture in this malady.—Ed.]

Chronic Tuberculosis

This disease, if accompanied by fever and severe inflammatory phenomena, usually gives rise to a polynuclear leukocytosis. The leukocytosis corresponds roughly to the degree of inflammation, and is accordingly slight or often entirely lacking in incipient tuberculosis. From his own experience the author cannot confirm the theory that the leukocytosis depends upon a mixed infection. One often finds a decrease in the numbers of the eosinophiles and lymphocytes, varying in degree with the severity of the condition. The hemoglobin percentage and the red-cell count are often diminished in incipient as well as in advanced cases, but by no means without exception. These rules obtain for all forms of tuberculosis, whether of the lungs, lymph-nodes, bones, intestines, or serous membranes. (In regard to Tuberculous Meningitis, see p. 800.)

Acute Miliary Tuberculosis

In this disease the leukocyte count, though sometimes diminished, is usually normal. Leukopenia is, therefore, of no value in differentiating it from typhoid fever.

Actinomycosis

Actinomycosis may give rise to leukocytosis if there be suppuration.

Syphilis

The present hematologic investigations seem to the aut or to be as yet quite insufficient, because the manifestations of syphilis are not sharply enough differentiated from one another. According to Sabrazès and Mathis, there is in the initial stage a normal count or a slight increase in the mononuclear cells—according to

[1] Zeit. f. Hyg. u. Infectionskrankheiten, vol. xlii, part 3.

Löper, a lymphocytosis. In the secondary stage (with general lymphadenitis) both Sabrazès and Nägeli found a polynuclear leukocytosis and a marked increase in the mononuclear cells and transition forms.

Suppurative Affections

Suppurative processes generally lead to a marked neutrophile leukocytosis. The character of suppurative leukocytosis in perityphlitis has been carefully studied, especially by Curschmann. He differentiates (1) Mild cases without leukocytosis or in which leukocytosis remains slight; (2) rather severe non-suppurative cases which present a transitory leukocytosis up to 22,000; and (3) severe suppurative cases which give rise to a high leukocytosis and which indicate operation. According to Curschmann, even a single leukocyte count of 25,000 is very suggestive of abscess formation, especially if it occur late in the disease. Although there are, of course, exceptions to these rules (absence of leukocytosis in very severe cases), yet, as the author pointed out in his communication to the Congress of Internal Medicine at Munich, 1895, such examinations are of great value, especially to observers of slight experience who might not realize the severity of a case from the general clinical picture. It is to be particularly emphasized, however, that one should not limit himself to a single count, but should control it by repeated examinations. In certain cases even two counts each day are to be recommended. Nägeli properly insists that not the severity of the infection, but also the reactive power of the bone-marrow, decides the degree of leukocytosis. If this be kept in mind, one will not be deceived by slight or even absent leukocytosis, but will regard it as an unfavorable sign in cases where the general clinical symptoms are severe.

Nägeli undertook an exact differential examination of the leukocytosis in perityphlitis. He found that in severe cases the eosinophiles are absent and that the percentage of lymphocytes is very low. According to this writer, any improvement soon manifests itself by the reappearance of the eosinophiles and an increase in the lymphocytes.

[Gibson,[1] in a critical study of the behavior of the leukocytes in appendicitis, reached the following conclusions: "The higher the polynuclear percentage as compared to the leukocyte count, the greater the probability of a purulent exudate. It is of value chiefly in indicating fairly consistently the existence of suppuration or gangrene. . . ." He describes a chart for representing the relation of the differential to the total count. According to Murphy,[2] a sudden fall in the absolute number of leukocytes with a slight decline or a rise in the percentage of polymorphonuclears is evidence of a severe infection.—Ed.]

It might be pointed out that Arneth's so-called "shifting of the neutrophile blood-picture," as well as the appearance of myelocytes observed by Schindler, are also to be considered as evidence of the severity of the infection (see below).

Leukocyte counts may be of similar practical value in the diagnosis and prognosis of pleural empyema, as well as in the diagnosis and prognosis of suppurative affections of the gall-bladder, of fat-necrosis and suppuration of the pancreas, suppurative gynecologic affections, suppurative puerperal infections, etc.

In regard to the iodin reaction of the leukocytes in suppuration see p. 787 et seq.

Trichinosis

See Eosinophile Leukocytosis, p. 808 et seq.

THE PRESENCE OF MYELOCYTES (Schindler) AND THE SO-CALLED SHIFTING OF THE NEUTROPHILE BLOOD-PICTURE IN INFECTIOUS DISEASES (Arneth)

These two studies are considered together, since both aim to show that in infectious diseases the character of the white cells, as well as their number, alters the blood picture, and that in some cases more comprehensive conclusions can be drawn from the qualitative differences than from the absolute number of the leukocytes alone. It was at first believed that conclusions as to prognosis could be drawn from the degree of leukocytosis, especially in pneumonia, in which leukocytosis has longest been recognized and best studied. This has, however, been proved impossible because, in consequence of the strong resistance of the organism, a high leukocytosis has been observed in mild infections that run a favorable course, as well as in the

[1] Annals of Surgery, April, 1906, p. 485.
[2] Keen's Surgery, vol. iv, p. 753.

gravest and most unfavorable cases in which the toxic irritation of the bone-marrow is intense. Thus, it appears that a slight leukocytosis may be a consequence of the lessened virulence of the pneumonic infection or of an insufficient reaction on the part of the organism. If the mere numbers of the leukocytes be considered, there results, in a way, an equation containing two unknown quantities which is impossible of solution. Another reason for the uncertain value of a mere leukocytosis is that, to a certain extent, an existing leukocytosis represents the balance between the demand for and the supply of leukocytes. Thus a definite degree of leukocytosis may result from an excessive supply and an excessive consumption of leukocytes (severe infection) as well as from a lessened supply and a diminished consumption of the same (mild infection). This statement also leads to an equation with two unknown quantities, the solution of which is necessary for the establishment of a prognosis. Both the writers make an effort to obviate these difficulties.

Schindler's Studies upon the Presence of Myelocytes in the Blood During Infectious Diseases

Besides fully developed leukocytes, Schindler[1] found also their undeveloped progenitors (the myelocytes) in the blood during leukocytosis. He rightly considered that the number of undeveloped cells presents a criterion for judging the demands made upon the bone-marrow, since manifestly only an intense toxic irritation of the latter can make such demands and cause the presence of such forms in the blood. Schindler expresses his results in regard to the finding of myelocytes in the blood in infectious diseases by the following propositions:

"1. The most varied causes (in particular those of an infectious nature) which excite leukocytosis are, in so far as they are permanent, those which give rise to a migration into the blood of large mononuclear cells with neutrophile granules (myelocytes) that normally never leave the bone-marrow. Thus we find myelocytes in pneumonia, scarlet fever, diphtheria, erysipelas, meningitis, polyarthritis, septic conditions, etc. Their mere occurrence is not always of the same significance. If they occur merely as an accompaniment of leukocytosis at the height of the same and disappear with its recession, we can infer nothing further than an insignificant expression of the ability of the bone-marrow to supply cells hastily, following the exhaustion of the existing reserves of developed leukocytes. If, however, myelocytes occur at a time when the leukocytosis has partially or quite receded, they bear witness to a functional exhaustion of the bone-marrow, the degree of which is indicated by their numeric relations to the developed cells. When the decrease in leukocytes is, together with the fall in temperature and the general symptoms of improvement, a sign of the victory of the organism over the infection, this transitory exhaustion is of no moment and is soon relieved. It is, however, of gravest significance if it supervene at a time when the infection is still fully virulent and when the organism is in greatest need of the supply of protective cells. Herein lie the grounds for the prognostic and, so to speak, practical value of the myelocytes as a measure of the normal power of the marrow to respond to stimulation. Great numbers during a falling leukocytosis and an unconquered infection are a bad sign (diphtheria, pneumonia).

"2. In the cases cited the cause of the defective leukocyte-production lies in the exhaustive paralysis which results from excessive demands (naturally, the marrow reacts at first because of its inherent properties, whether or not it becomes insufficient later). Thus, in typhoid and in malaria the cause of the leukopenia is a direct arrest of the function of the leukocyte-forming tissue through the specific influence of the toxins due to the disease—an arrest which in one case (typhoid) is permanent, in the other (malaria) is only temporary. Here again we conceive the myelocytes to be evidence of an abnormal reaction of the bone-marrow to stimulation."

Arneth's Neutrophile Blood-picture; Anisoleukocytosis

Arneth,[2] starting with the same ideas as Schindler (see above), undertook to make a further differentiation among the neutrophile leukocytes (formerly classed together) according to the number of nuclei, and to make this differentiation of clinical value. He used in his examinations dried smears which were fixed in absolute alco-

[1] Schindler, Studies on the Presence of Myelocytes in the Blood, I. A. D., Bern, 1904, and Zeit. f. klin. Med., 1904, vol. liv.

[2] Die neutrophilen weissen Blutkörperchen bei Infectionskrankheiten, Jena, Fischer, 1904.

hol for one hour and then stained for one and one-half minutes in triacid solution. Beautiful preparations were thus obtained in which even the nuclei were satisfactorily stained. In order to exclude digestive leukocytosis he took the blood either before breakfast or before the principal meal of the day.

As is well known, the terms polymorphonuclear and polynuclear are used loosely, since there are all types of transition forms between the cells in which the nuclei are quite separate and those in which they are connected by more or less broad bands. In opposition to this tendency Arneth sharply differentiates cells with one nucleus and those with two, three, four, five, or more nuclei or divisions of the nucleus. He classes myelocytes as mononuclear forms of the polymorphonuclears (p. 791), though the former are usually considered separate from this type. According to Arneth and in accord with the classification on p. 790, the remaining mononuclear forms of neutrophile leukocytes represent transition forms between myelocytes and true polynuclears. Among these transition cells Arneth differentiates those with slightly indented and those with deeply indented nuclei. He further subdivides the cells with more discrete nuclei according to the number of spheric or loop-shaped parts, a classification of less interest, which need not be considered here. Now, Arneth found that these individual types follow definite laws in normal and pathologic cases. The following table, selected from one of Arneth' examples, represents the normal neutrophile blood-picture. It should be noted that he designates the myelocytes by *M*, cells with slightly indented nuclei by *W*, and those with deeply indented nuclei by *T*.

1 nucleus. *M W T*	2 nuclei.	3 nuclei.	4 nuclei.	5 or more nuclei.	
7	39	36	16	2	= 100 per cent.

The absolute numbers represent the percentages, since Arneth always constructs his tables from a count of 100 cells in a smear. In order to understand the literature, it should be noted that loop-shaped parts of the nuclei are represented by *S* and spherical parts by K.

The leukocytes with two and three nuclei (Arneth's second and third subdivision) normally preponderate, as is seen in the above table. Pathologically, especially in infectious diseases, this relation is strikingly altered (or shifted) so that the number of cells to the left of the table is increased at the expense of those to the right. Arneth calls this the "shifting of the neutrophile blood-picture toward the left," and since he regards polynuclears as older and matured descendants of the mononuclears, he assumes that this shifting is brought about by the retirement of the developed cells in favor of the immature ones, just as earlier writers, especially Schindler, interpreted the appearance of myelocytes in infectious diseases. The following blood-picture obtained by Arneth in a case of angina with pneumonia is an example of such a shifting:

1 nucleus. *W M T*	2 nuclei.	3 nuclei.	4 nuclei.	5 or more nuclei.	
21	54	32	2	1	= 100 per cent.

These qualitative changes, as Arneth shows, are quite independent of the absolute number of leukocytes. Consequently, he undertakes to make the following classification of the pathologic variations in the neutrophile blood-picture, taking into consideration the presence of different combinations of the qualitative and quantitative changes. By the term isocytosis he means a normal percentage of the several varieties of neutrophile leukocytes; by anisocytosis, a qualitative change or "damage" to the normal relation.

1. Hyperleukocytosis or hypercytosis, an increase of the neutrophile leukocytes:
   (*a*) Isohypercytosis, an increase without qualitative changes.
   (*b*) Anisohypercytosis, an increase with qualitative changes.
2. Normoleukocytosis or normocytosis, a normal leukocyte count.
   (*a*) Isonormocytosis, the same without qualitative changes.
   (*b*) Anisonormocytosis, the same with qualitative changes.
3. Hypoleukocytosis or hypocytosis, a decrease in the leukocyte count.
   (*a*) Isohypocytosis, the same without qualitative changes.
   (*b*) Anisohypercytosis, the same with qualitative changes.

Arneth sees the cause of the anisocytosis or shifting of the blood picture to the left in the destruction of the developed leukocytes by the bacterial toxins combined with the supply of immature cells. The chief interest of Arneth's studies lies manifestly in the possibility of demonstrating changes in the neutrophile leukocytes, *i. e.*,

injury to the blood in infectious diseases where there is neither leukocytosis nor leukopenia, and further in demonstrating that normo-, hyper-, and hypoleukocytosis may possess a common qualitative characteristic (anisocytosis), in spite of their quantitative differences. Unfortunately, however, these new methods of study throw but little light on diagnosis and prognosis—manifestly not on the latter, because they have the same value as counting the absolute number of leukocytes. Indeed, marked anisocytosis may signify a very severe intoxication or a very favorable reactive power of the bone-marrow, *i. e.*, a well-marked resistance on the part of the organism. From observations extant we have no means of telling which of these diametrically opposed conditions it indicates. Both favorable and unfavorable cases may exhibit decided anisocytosis. For the findings in individual diseases the reader is referred to Arneth's original work.[1] The hyperleukocytosis of most infections is an anisohyperleukocytosis, just as the leukopenia caused by such diseases as typhoid and measles is an anisohypocytosis. In protracted cases of pneumonia with delayed resolution there may be anisonormocytosis, though the absolute count shows no abnormality. There is a long-continued anisonormocytosis during convalescence from measles. Isohypercytosis occurs during digestion and after cold baths and occasionally in articular rheumatism and tetanus.

Arneth's method is exacting and tedious. Numerous attempts have been made to simplify it; and, indeed, this may be done by counting (as Wolf recommends) the number of nuclei or parts of nuclei in 100 individual cells and, instead of tabulating the leukocytes according to the number of nuclei, reckoning the average, a decrease in which corresponds to shifting of the neutrophile blood-picture to the left. The advantage of this method is that changes in the blood-picture during the disease can be clearly represented by a simple curve of the average number of nuclei. Instead of this Kothe[2] advises counting the number of mononuclear leukocytes alone and expressing their percentage of the total leukocytes. This procedure resembles Schindler's examinations, since the myelocytes are included in counting the mononuclear cells.

Pollitzer[3] and others have raised the objection that there is no proof that a decrease in the number of nuclei or parts of the nucleus is a mark of the immaturity of the cell and not a sign of the clumping of the divisions of a previously many-parted nucleus, due to injury. He also calls attention to the fact that the triacid stain which Arneth uses, being an imperfect nuclear stain, makes a clear differentiation difficult, and that with other, better, nuclear stains, cells with only one or two nuclei are not found. According to many later studies, however, there is something real at the bottom of Arneth's findings in whatever way these findings may be explained and whether one concede a diminution in the number of nuclei or merely a clumping of the divisions of the same. Besides Arneth's theory is in close accord with results of Schindler's studies on myelocytes if it be assumed that the cells with few divisions of the nucleus represent transition forms between myelocytes and mature leukocytes. The author does not wish to join in the debate, but would remark that, so long as the above objections to Arneth's examinations are maintained, Schindler's studies possess a firmer basis, since myelocytes are more surely differentiated in well-stained and even triacid preparations and are recognized as the ancestors of the neutrophile leukocytes. It is remarkable that though Arneth's findings have been rather exhaustively discussed, very little attention has been paid to Schindler's studies. This is due chiefly to the fact that myelocytes are, as a rule, so few (usually only a fraction of 1 per cent., and even in pneumonia and malaria only as high as 1.6 per cent. and 2.5 per cent. respectively) that one must count very many leukocytes in order to form a proper judgment of the proportion of myelocytes. Later investigators, however, have found higher and easily determined percentages of these cells; thus in diphtheria Engel found 10 per cent., and in sepsis complicated by anemia Nägeli found 25 per cent.

OTHER POLYNUCLEAR NEUTROPHILIC LEUKOCYTOSES

Toxic and Medicinal Leukocytosis.—This is observed chiefly in poisoning with the blood-poisons, potassium chlorate, phenacetin, and arsenic, after chloroform, and in hemoglobinuria. These conditions have not been especially studied.

[1] See the monograph cited above, Münch. med. Woch., 1904, No. 45; Zeit. f. klin. Med., 1905, and Die Lungenschwindsucht auf Grund klinischer und hämatologischer Untersuchungen, Leipzig, Barth, 1905. In the last a number of other works are quoted.

[2] Berlin. klin. Woch., 1908, No. 36, p. 1633.

[3] Wien. klin. Woch., 1906, No. 4, and Arch. f. klin. Med., 1907, vol. xcii.

Among the drugs which produce a polynuclear neutrophilic leukocytosis when used internally are antipyrin and antifebrin. The pilocarpin leukocytosis seems to be mainly a lymphocytosis. (See p. 809.)

Tuberculin injections lead to a leukocytosis, the appearance of which, according to the author, is associated with, and a much more delicate test than, the other phenomena of a reaction. Blood-examination may, therefore, be used with advantage to control tuberculin injections for therapeutic purposes. They are much simpler and less time consuming for this purpose than Wright's estimation of opsonins. The author's observations in this regard are based upon Beraneck's tuberculin. Fanconnet does not confirm the lymphocytosis and eosinophilia which some writers have insisted follow the use of tuberculin.

Anemic Leukocytosis.—This is observed chiefly after acute loss of blood (posthemorrhagic leukocytosis) and in those types of anemia where the bone-marrow is in a state of increased regenerative activity (secondary anemia). The polynuclear neutrophilic cells are chiefly affected. The leukocytosis may be very marked. It disappears when the loss of blood has been replaced by regeneration.

Cachectic Leukocytosis.—This is polynuclear and neutrophilic, and is observed chiefly in malignant tumors—carcinoma and sarcoma.

Agonal Leukocytosis.—This has been observed shortly before death from various diseases, even in those which in themselves, as a rule, produce no leukocytosis. Ehrlich and Lazarus do not regard this as a true leukocytosis, but claim that the white corpuscles are deposited in the peripheral vessels on account of the general depression of the circulation. This accumulation affects chiefly the polynuclear neutrophiles.

EOSINOPHILE LEUKOCYTOSIS, OR EOSINOPHILIA

This is not only a relative, but an absolute, increase of polynuclear eosinophilic leukocytes. The total leukocyte count may be normal or increased. In the latter case the neutrophiles are also usually increased. This condition may be called eosinophilia plus neutrophile leukocytosis, whereas an increase in the eosinophiles alone may be termed simply eosinophilia. The number of eosinophiles is normally 140 to 280 per cubic millimeter, *i. e.*, 2 to 4 per cent. of the total number of leukocytes. They may increase up to 5000. It must be borne in mind, in estimating the degree of eosinophilia, that the eosinophiles are more numerous in children than in adults. A pathologic eosinophilia is observed:

1. In *bronchial asthma* and "eosinophile" bronchitis, which occurs especially in emphysema. The eosinophiles may be increased up to 20 per cent. of the total number of leukocytes.
2. In *pemphigus*, Zappert found 4800 eosinophiles in a cubic millimeter.
3. In various other *cutaneous diseases* (urticaria, prurigo, eczema, mercury dermatitis). Lazarus found 60 per cent. of the leukocytes to be eosinophiles in a case of urticaria.
4. In *multiple blastomycosis* (yeast-fungus infection) Harter and Lucien found an eosinophilia of 18 to 23 per cent. of the general leukocytosis.
5. In certain forms of *neurasthenia* and nervous diarrheas (Nägeli).
6. In *helminthiasis* [ankylostoma, ascaris, oxyuris, bothriocephalus, tenia, anguillula stercoralis and intestinalis (strongyloides intestinalis), trichocephalus, and perhaps in other intestinal parasites, as well as echinococcus and cysticercus, trichina, filaria sanguinis, distomum hæmatobium (bilharzia)]. Eosinophilia has been observed in intestinal helminthiasis, especially when Charcot's crystals are present in the stools (p. 521 et seq.). The diagnostic significance of this finding is manifest. The eosinophiles disappear immediately after the death of the echinococcus.[1] According to the last writer, persistence of eosinophilia after operation indicates the presence of still unopened cysts. The eosinophiles disappear if the disease (ankylostomum, bothriocephalus, and rarely tenia and trichocephalus) causes too severe an anemia. The author's observations, however, do not agree with the statement that eosinophilia is absent (especially in bothriocephalus disease), even before anemia supervenes. The truth is that in this infection eosinophilia is not so constant as in the other forms of helminthiasis. For the complete blood-picture caused by these parasites see p. 840 et seq.

In *trichinosis*,[2] since eosinophilia is present in the overwhelming majority of

[1] Chauffard and Bodin, Bull. de la soc. med. des hôp., 1907, p. 1473, and Rossello, Comptes rend. de la soc. de biol., 1907, lxiii, p. 423.

[2] [Brown, Johns Hopkins Hospital Bull., April, 1897, was the first to call attention to the diagnostic value of eosinophilia in trichiniasis.—Ed.]

these cases, it is of the greatest diagnostic importance,[1] especially in differentiating this affection from typhoid fever, in which the eosinophile cells entirely disappear at the height of the disease. In trichinosis the number of eosinophile leukocytes after the fourteenth day may be increased to 40 to 50 per cent. of the total number (Schleip). The absolute number of total leukocytes is not always increased. In 7 cases of human trichinosis Stäubli also found a very high percentage of eosinophiles. In animal experiments the eosinophilia appeared on the seventh day after the ingestion of infected meat. Stäubli found a very high general leukocytosis in severe cases in man. The neutrophiles as well as the eosinophiles are increased in numbers. The lymphocytes behave as in typhoid, *i. e.*, they are first diminished and then persistently increased in numbers. In both men and animals the occurrence of polycythemia and polychromemia has been demonstrated at the beginning of the infection. Later on this condition gives way to a slight grade of anemia. In severe cases, as well as in mixed infections, the eosinophiles may be absent or may disappear after persisting for a short time. In regard to the possibility of the occurrence of trichina embryos in the blood see p. 822 et seq.

7. *Post-febrile Eosinophilia.*—After the disappearance of the fever in many infectious diseases, especially if accompanied by the ordinary neutrophile leukocytosis (pneumonia, acute rheumatism, malaria). In scarlet fever the eosinophiles are increased not only after the fever has vanished, but during the fever also. In regard to the alleged eosinophilia after injection of tuberculin see p. 808.

8. In malignant tumors leading to cachexia.

9. After removal of the spleen and in chronic tumors of the spleen.

LYMPHOCYTOSIS

This name is applied to those conditions of the blood where there is an increase of lymphocytes, but it does not include the lymphocytosis of lymphatic leukemia, which is sufficiently characteristic to be termed an independent disease. We know very little as yet about the occurrence of a pure lymphocytosis. It should be mentioned, however, that in some conditions or ordinary polynuclear leukocytosis, for instance, in the leukocytosis of digestion, the lymphocytes may also be increased, and that in the new-born the physiologic leukocytosis is a lymphocytosis. Pathologically, a lymphocytosis occurs in whooping-cough (p. 802) and in a certain stage of typhoid (see p. 799), as well as at the end of many other infections. (See p. 797 et seq.) Lymphocytosis has been observed after injection of pilocarpin. A lymphocytosis is of an entirely different clinical significance from a polynuclear leukocytosis, not only because the former cells are derived from the lymphatic glands and have a function quite different from the latter, but also because, on account of their slightly developed ameboid contractility, their origin must be attributed, according to Ehrlich and his school, rather to a mechanical washing out of the lymphocytes from the lymphatic glands, and to anatomic changes in the latter structures than to chemotactic irritants in the blood. In contradistinction to the earlier supposition, it should be noted that recent observations indicate that the lymphocytes are by no means immobile.

In regard to the alleged lymphocytosis following tuberculin injections see p. 808.

BLOOD-PLATELETS

Bizzozero and Hayem have recently demonstrated that the granules and clumps of granules visible in any fresh blood-preparation are postmortem formations which owe their existence to rapid disintegration of the elements called blood-platelets or hematoblasts.

[1] See Schleip, 75, Naturforscherversammlung, 1903, ref. in Berlin. klin. Woch., 1903, No. 41, p. 946, and Arch. f. klin. Med., vol. lxxx, and Stäubli, Deut. Arch. f. klin. Med., 1906, vol. lxxxv, pp. 286–341.

These blood-platelets (Pl. 7, Fig. 41) are small, circular or oval, colorless structures, about 3 μ in diameter. They disintegrate very easily, and adhere very readily to each other and to the other elements of the blood. They play an important part in the etiology of white thrombi. Their number is variously estimated at from 200,000 to 500,000 per cubic millimeter. If only elements which are stained by methyl-violet are counted, their number, according to the estimations made at the author's clinic, varies between 150,000 and 200,000. In harmony with Bizzozero, Deckhuyzen and Deetjen have shown the corpuscular character of the platelets and the presence of nuclei in them, and have sharply differentiated them from certain structures arising from the disintegration of leukocytes and red cells with which they were formerly confused.

For the purpose of examining blood-platelets before they are destroyed, it is necessary to add some preservative fluid to the blood the moment it is drawn. Hayem recommends the following:

(1) A solution of 1 part of methylene-violet and 5000 parts of 75 per cent. (physiologic) solution of sodium chlorid. (See, however, p. 768.)

(2) A mixture of 1 part of a 1 per cent. aqueous solution of osmic acid and 2 parts of 0.75 per cent. solution of sodium chlorid. The latter fluid fixes the blood-platelets permanently, whereas the former stains them. Bizzozero puts a drop of one of these solutions on the finger-tip, the skin of which has been carefully cleansed. The skin is then punctured through the fluid, so that the elements of the blood come in immediate contact with the fluid. This blood-mixture is placed under the microscope; the characteristic blood-platelets are then seen, but no granules.

A much better method which permits the demonstration of their disputed ameboid movements is as follows: Blood obtained by puncturing a vein is collected in a small graduate containing a solution of 0.001 gm. hirudin in 5 cc. water. After it has stood a short time a smear is made from the upper layers which is free from corpuscles, but swarming with platelets. A cover-slip rimmed with vaselin is placed on the smear, and the latter is examined on a warm stage with the oil immersion. The ameboid movements of the platelets as well as their morphology can be observed.

Formerly, blood-platelets were counted in a very similar way to the red blood-corpuscles. Bizzozero, however, believes that if this method of counting blood-platelets be used, a considerable number adhere to the side of the pipet. He, therefore, advises that the blood be received directly into a 14 per cent. solution of magnesium sulphate, according to the technic described above. The blood-platelets are a little deformed, to be sure, but this solution, by coagulating their protein, reduces their tendency to clump, and, therefore, keeps them isolated. The ratio between red blood-corpuscles and blood-platelets can then be estimated by the Thoma-Zeiss counter, the number of red blood-corpuscles determined in the usual way, and the absolute number of blood-platelets then reckoned. Bizzozero's method is followed at the Bern clinic with the modification of adding to the 14 per cent. magnesium sulphate solution enough methyl-violet to stain the platelets, and only those elements thus stained are counted (see above). Affanasiew has recommended the use of a solution consisting of 0.6 per cent. sodium chlorid with 0.6 per cent. peptone and a little methylene-violet. The number of blood-platelets may also be found by a determination of the ratio between it and the number of the leukocytes in a dry preparation; the disadvantage of this method is that the blood-platelets are found, clumped, and are not always easy to distinguish from precipitate.

These methods of blood-platelet-counting possess many difficulties, the greatest of which is that the platelets cannot always be absolutely differentiated from disintegration products of the other formed elements of the blood. Besides, it may be that because of their small size they do not fall promptly to the bottom of the counting chamber, and must, therefore, be looked for at different levels of the fluid. Further, it is impossible to employ the powerful objectives which are essential for exact recognition of the platelets, because of the depth of the ordinary counting-chamber. Helber[1] has devised a method which overcomes these difficulties. He uses a counting-chamber[2] which is only 0.02 mm. deep. With this cell and the accompanying thin cover-slip the stronger objectives (preferably Zeiss E) may be used, and with a compensating ocular (No. 12) a magnification of 1080 diameters, which is sufficient to distinguish platelets from similar structures can be obtained, ocular (No. 6) is practically strong enough. Helber makes a dilution of 1: 30 in a specially constructed pipet, using a 10 per cent. solution of sodium metaphosphate, which preserves the platelets well. When a drop of the dilution is placed in the counting-chamber, the platelets can be easily recognized among the red cells as colorless bodies one-third the

[1] Deut. Arch. f. klin. Med., vol. lxxxi, p. 316.

[2] Made by Zeiss in Jena.

size of the latter, round or oval in shape, and with a darker central portion, the nucleus. A satisfactory dilution must appear in the ampulla of the pipet to be clear by transmitted light and slightly turbid (ground color) by strong direct light. In Helber's counting-chamber one can count red cells, platelets, and leukocytes at the same time, though the number of the latter is hardly sufficient on account of the shallow cell. By this method Helber found about 200,000 to 250,000 plates per c.mm., which corresponds approximately to earlier estimates.

[Pratt[1] recommends the following technic: A clean platinum loop is filled with a 2 per cent. solution of sodium metaphosphate in physiologic salt solution and just touched to the top of a drop of blood obtained by pricking the lobe of the ear. The mixture is transferred to a slide and at once covered with a clean cover-slip. The ratio of platelets to red blood-corpuscles is then determined, and from the actual number of red corpuscles, counted in the usual way, the actual number of platelets is estimated. J. H. Wright counts the actual number of platelets as follows: The blood from a finger-prick is diluted 1 : 100 in a red-cell pipet with a mixture of equal parts of a solution of brilliant cresyl blue (1 : 300) and potassium cyanid (1 : 1400), the pipet is well shaken, and a drop placed in the counting-chamber and covered with a very thin, specially made cover-glass. One must wait at least ten minutes to allow the platelets to settle before counting.—Ed.]

Little is as yet known regarding the relation of blood-platelets to pathologic conditions. According to Bizzozero, they are increased in pregnancy, after the loss of blood, in chlorosis, in tuberculosis, cholera, etc. They are diminished in the fever of acute diseases, but, according to Hayem, increase toward the end of a fever (crise hématoblastique). Denys observed a diminution of blood-platelets in purpura. Helber found them increased in mild anemias and diminished in the severe irreparable forms of anemia. (See p. 781 with reference to the Iodin Reaction of Blood-platelets.)

HEMOKONIA OR BLOOD-DUST

Blo d-dust and hemokonia are names given to very minute granules which are always found in the blood and blood-serum. They are the size of the smallest bacteria, therefore much smaller than platelets and not to be confused with them. They exhibit Brownian movement. Their composition is still under discussion; in any case they consist in great part of fat (see Lipemia). Some of them, however, stain with nuclear dies and are, therefore, thought to be derived from nuclei. Their origin has even been thought to be the granules of the leukocytes. In regard to the literature, see Nägeli's works.[2]

MELANEMIA

By *melanemia* is meant the presence of granular brownish or black pigment in the blood. It is usually found in the interior of white blood-corpuscles, which are often irregular in shape, and less frequently as free plates between the cellular elements of the blood. Melanemia has as yet been found only following malaria, especially long-continued malarial cachexia, and in recurrent fever. In malaria (see pp. 802 and 819) the pigment derived from hemoglobin may show all shades of color from red to black. The presence of white blood-corpuscles with pigment or of free pigment is of great diagnostic importance in those cases in which the malarial parasites are not readily demonstrable.

LIPEMIA

Blood always contains some fat under physiologic conditions. More marked lipemia is observed physiologically during digestion, and pathologically in chronic alcoholism, in acute phosphorus-poisoning, in severe diabetes, and in fractures which lead to fat-emboli. If the blood contain a considerable amount of fat, its pallor and cloudiness are apparent to the naked eye. Under the microscope the fat is usually seen in the form of very fine granules (blood-dust), just as in chyle: in embolic lipemia distinct light-refracting droplets may be seen. They are stained black by osmic acid, and red by Sudan III, and dissolved in a dry preparation by the addition of ether.[3] Even absolutely clear serum obtained from fasting individuals contains fat. It must be supposed that this is either dissolved in some unknown way or that it is present in a colloidal state or so finely emulsified that it is invisible.

[1] Jour. Amer. Med. Assoc., Dec. 30, 1905, p 1999.
[2] Nägeli, Blutkrankheiten und Blutdiagnostik, Leipzig, Veit and Co., 1908.
[3] Rieder, Arch. f. klin. Med., vol. lix, p. 444.

In a recent study of physiologic or digestive lipemia E. Neisser and H. Bräuning[1] reach the following conclusions: (1) The blood-serum of a man after a twelve-hours' fast is clear. (2) In the clear serum of a fasting man fat is present in solution or as a colloid or in such fine suspension that it cannot be perceived. (3) After the ingestion of a moderate amount of fat (equal to that taken in an ordinary meal) the serum is turbid; after any other food, clear. (4) In order to obtain clear serum the blood must be withdrawn after the patient has eaten no fat for twelve hours. (5) The turbidity of the serum after the ingestion of fat is due to an extremely fine suspension of this substance therein (hemokonia). (6) A layer of fat is formed in the serum after butter has been administered, from the thickness of which one may form an estimate of the hemokonia content. (7) The turbidity begins one to two hours after administration of milk-fat, reaches its height in about six, and disappears in eight to ten, hours. (8) The degree of turbidity varies with the kind of fat ingested and with the species of animal which ingests it. (9) In pathologic cases with diminished fat absorption the serum does not become turbid after the administration of fat.

The author would call attention to the significance of this last fact in the diagnosis of pancreatic disease and in cases when the bile in the intestine is diminished.

THE DEMONSTRATION OF BACTERIA IN THE BLOOD

DIRECT MICROSCOPIC DEMONSTRATION OF BACTERIA IN THE BLOOD

To demonstrate bacteria in the blood directly, dry preparations may be spread between two cover-slips in the usual way. It is even better to use slides, so that the largest possible amount of blood may be studied. Such preparations can be exam-

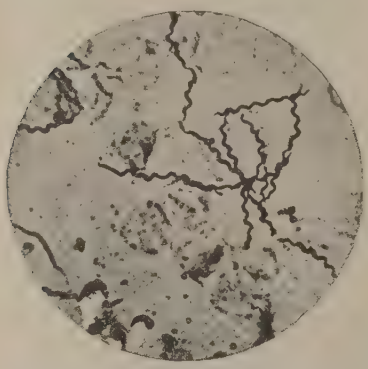


Fig. 308.—Spirochætæ of relapsing fever (Spirochæta Obermeieri) in blood. Photograph by Weichselbaum (× 1000).

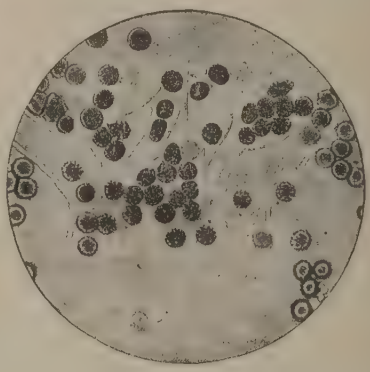


Fig. 309.—Anthrax bacilli in blood, unstained (× 430) (Fränkel).

ined without cover-slips. The slides are fixed by passing them through the flame two or three times, and then stained like specimens of sputum. (See pp. 709, 715 et seq.)

Since the staining of the erythrocytes and of the dried albumin of the blood interferes with the beauty and transparency of the preparations, the procedure suggested by Günther[2] may be followed with advantage, as by it the hemoglobin and part of the albumin are removed from the dried specimen. Günther fixes the dried blood by heat, and then washes it for ten seconds in a 5 per cent. solution of acetic acid. The cover-glass is then dried, and for several seconds its smeared side is held directly over an open bottle of ammonia, which has been previously well shaken, so that the last remains of the acid may be neutralized. It is now immersed in the staining solution for a short time and then washed in water. Since the tinctorial characteristics of the erythrocytes depend upon their contained hemoglobin, these structures will appear colorless, and any bacteria present will be easy

[1] Zeit. f. exper. Path. u. Therap., 1907, vol. iv.
[2] Fortschritte der Med., 1885, vol. iii, p. 756.

of recognition. Nöggerath's and Stähelin's centrifuge method for demonstrating Spirochæta pallida (p. 816) may be of service in demonstrating also small numbers of bacteria in the blood.

Another method, devised by Löper and Louste,[1] consists of mixing a drop of blood with 1 cc. absolute alcohol and 2 cc. distilled water and centrifuging. The red cells are thus dissolved and bacteria can be demonstrated in dry preparations of the sediment.

The *bacilli of anthrax* (Fig. 309) are pathognomonic when found in the blood. They may be recognized in unstained specimens. For culture methods, see p. 814.

Bacteria are more easily demonstrated in the blood by cultures than by a microscopic examination, *e. g.*, the streptococci and staphylococci (compare Figs. 284 and 285) found in septicopyemia. The number of micro-organisms found in the blood is always comparatively small, so that considerable blood should be employed to inoculate the culture medium. For this purpose a sufficient quantity of blood is removed from some vein of the arm with the aid of a small syringe fitted with an asbestos piston and thoroughly sterilized. This syringe should contain about 5 cc. The skin should be first carefully disinfected with alcohol and corrosive sublimate. About 1 cc. of this blood is added to a tube of agar (liquefiable at 40° C. at the most), to one with 10 per cent. gelatin, and to two bouillon tubes. The fluids are carefully shaken, and the agar and the gelatin tubes are plated. The agar plates and the bouillon tubes are placed in the incubator at 37° C., the gelatin plate at 22° C., Sittmann[2] found pus-cocci or staphylococci in the blood in every case of septic pyemia which he examined in this way. The bacteriologic examination of the blood is the most accurate aid for determining pyemia.

In severe cases of pneumonia we have not infrequently been able to demonstrate pneumococci in the blood by direct microscopic examination of dry preparations. This shows the relationship existing between pneumonia of the human subject, which is usually regarded as a purely local affection, although it is really very often accompanied with a general blood infection, and the pneumococcic sepsis of laboratory animals. Günther's process, given upon p. 812, for the removal of the hemoglobin with acetic acid, greatly aids the demonstration of the capsules of the pneumococci. Wiens (see below) considers that pneumococci can be demonstrated in the blood of most all patients with pneumonia provided his culture method be employed (fluid media).

Typhoid bacilli may frequently be demonstrated in the blood of typhoid fever patients, either in fresh specimens or in cultures, and, as the author can testify, may even be found in cases running a mild course. They are most frequently found in the first week of the disease.

Pöppelmann[3] claims that even quite early in the disease typhoid bacilli can be found in the blood if a number of smears from a large drop of blood be examined. He uses Jenner's stain (see p. 778 et seq.), without special fixation. The bacilli are colored blue. The culture method, however, is more often successful (see below).

Even *meningococci* have been demonstrated in the blood of patients with epidemic meningitis (Rusca, in the author's clinic).

The demonstration of *pest bacilli* Fig. (289) plays an important rôle in the diagnosis of bubonic plague. (For their recognition the reader is referred to the section upon Examination of the Sputum.)

The occurrence of the *Bacillus mallei* (p. 721) in the blood is of less diagnostic importance.

Tubercle bacilli (p. 709) have as yet been found in the blood only in acute miliary tuberculosis, and then in very small numbers.

Staphylococci and *streptococci* can, as a rule, be recovered from the blood only by culture. (See p. 719 et seq.)

Micrococcus melitensis (Bruce), which is the cause of Malta fever (a disease occurring in Malta, the Mediterranean countries, India, China, and Japan), can sometimes be demonstrated in the blood. It is a very small organism (about 0.3 μ in diameter), elliptic in form. It is doubtful whether it should be described as a coccus or a short bacillus. It is non-motile and Gram-positive. Scanty growth can be obtained on agar. It does not liquefy gelatin. It is best recovered from the blood by culture. The agglutination test is also of importance (p. 862).

[1] Arch. de med. exp., vol. xvii, part 3.

[2] Deut. Arch. f. klin. Med., 1894, vol. liii, p. 327; see Petruschki, Zeit. f. Hyg. u. Infectionskrankh., vol. xvii, p. 59.

[3] Deut. med. Woch., 1906, No. 24, p. 947.

CULTURAL DEMONSTRATION OF BACTERIA IN THE BLOOD[1]

In many cases bacteria can be demonstrated in the blood only by culture. This is particularly true of staphylococci and streptococci. Since they are often present in small numbers, a large amount of blood must be used in order to insure satisfactory results. Sittmann[2] recommends the following procedure: By means of a sterile syringe with an asbestos plunger, 5 cc. of blood are withdrawn from a distended vein in the bend of the elbow after careful disinfection of the skin with alcohol and bichlorid solution. One cc. of this is placed in nutrient agar, which has been liquefied and then cooled to 45° C., 1 cc. in nutrient gelatin (containing at least 10 per cent. of gelatin), and the remainder in 2 tubes of bouillon. The contents are immediately mixed by gentle agitation so as to avoid foaming, and the gelatin and agar tubes emptied into Petri dishes. The agar plate and the bouillon tubes are kept at 37° C. The gelatin plate is inverted to prevent the washing away of the colonies by the water of condensation and kept at 22° C. Lenhartz[3] uses still larger amounts of blood. This writer withdraws 20 to 30 cc. by means of a 30 cc. syringe with a glass plunger (Luer), and a cannula 6 to 7 cm. long and of not too small a bore, both sterilized dry.[4] After the vein has been entered the blood flows in without suction by virtue of its own pressure and displaces the plunger. The blood obtained is divided among 3 liquefied gelatin tubes and 3 tubes containing at least 10 cc. each of a liquefied agar cooled in a water-bath to 45° to 43° C. The blood and media are then mixed as uniformly as possible, care being taken to prevent foaming; each individual tube is emptied into a Petri dish, the gelatin plates kept at room temperature, and the agar plates at incubator temperature. In order to obviate any disturbances caused by the water of condensation, the covered plates are put away bottom upward. The growing colonies are easily seen by transmitted light. They usually seem to be dark green, but this, as the author has convinced himself, is merely because they are contrasted with the intense red of the blood-containing layers of the medium. Virulent streptococci are characterized by the fact that they deprive the medium of color in the immediate vicinity of the colonies. Non-pathogenic streptococci do not do this. (See p. 720.)

Wiens[5] has pointed out that the employment of fluid media is much more advantageous than the Sittmann-Lenhartz plate method, especially for the demonstration of pneumococci, since the results are much more frequently positive; indeed, according to Wiens, constantly so. He recommends an aqueous solution of 1 per cent. pure commercial peptone and 1 per cent. of dextrose. The reaction of the medium should be only very slightly alkaline. At least 1 cc. of blood is mixed with each tubeful of this fluid medium. After twenty-four hours' growth the culture is streaked on agar plates. The obvious disadvantages of this method are that no sure estimate of the numbers of bacteria can be made, and that errors may easily arise through contamination. The latter, however, may be avoided if several tubes be inoculated and if only similar results be credited.

Kayser and Conradi have recommended the culture of typhoid bacilli on sterilized bile to facilitate their growth, and the preparation of agar plates from this culture.

In accord with the fact that pneumococci, in contradistinction to streptococci, are disintegrated by bile[6] (the only point of difference between the former and certain forms of the latter), Wiens found that pneumococci could not be cultured from the blood if bile media were used.

[A simple procedure, if it be desired to cultivate the organism on several media, is to collect the blood at the bedside in a sterile solution containing 2 gm. ammo-

[1] [The reader is referred to the work of the following writers on blood-cultures: Libman, Amer. Jour. Med. Sci., Oct., 1908, p. 548; Johns Hopkins Hospital Bull., July, 1906, p. 215; Cole, Blood-cultures in Pneumonia, ibid., June, 1902, p. 136; Peabody, The Diagnosis of Typhoid Fever by Cultures from Blood of the Ear, Arch. Int. Med., Feb., 1908, p. 149.—Ed.]

[2] Deut. Arch. f. klin. Med., 1894, vol. liii, p. 327. See also Petruschki, Zeit. f. Hyg. und Infectionskrankh., vol. xvii, p. 59.

[3] Septic Diseases in Nothnagel's System, Spec. Path. u. Therap.

[4] In the author's clinic the syringe is placed in a lamp chimney, both ends of which are closed with gauze, and sterilized by one-half hour of dry heat (160° C.). It is then ready for use and may be kept as long as desirable.

[5] Zeit. f. klin. Med., 1908, vol. lxv, p. 53.

[6] For the diagnostic value of this fact see Sputum Examination, p. 717.

nium oxalate and 6 gm. sodium chlorid in 1 liter of water[1] or in a 1 per cent. solution of sodium citrate, and to distribute the mixture among the various media in the laboratory.—Ed.]

THE DEMONSTRATION OF SPIROCHÆTÆ IN THE BLOOD

Spirochætæ are screw- or spiral-shaped organisms whose biologic classification is uncertain. They were formerly classed as bacteria, while recently the tendency has been to regard them as protozoa,[2] or at least a group between the protozoa and bacteria, on the boundary line between the animal and vegetable kingdoms. The question cannot yet be definitely decided. The old name spirilla, which is still used here and there, should be replaced by the new term, spirochæta, since the use of the former causes confusion with the species spirillum of the genus bacteria. Spirochætæ were indeed formerly included in this species of the bacteria because they resemble the spirilla in form.

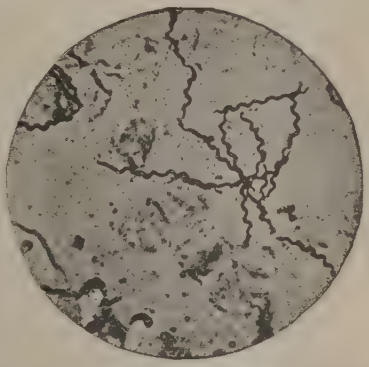


Fig. 310.—Spirochæta of relapsing fever (Spirochæta Obermeieri) in the blood. Microphotograph after Weichselbaum (1000 × 1).

Spirochæta Obermeieri (Spirochæta of Relapsing Fever, Formerly Called Recurrens Spirilla).—This micro-organism (see Fig. 310), discovered by Obermeier as far back as 1868, is the cause of relapsing fever (relapsing typhus, febris recurrens, or, briefly, recurrens), a disease formerly wide-spread throughout Europe, but since the Seven Years' War, present only in European Russia, and to a greater extent in Asia and in Africa. It is characterized by the alteration of febrile and afebrile periods (see curve, p. 82), by enlargement of the spleen, and frequently by a slight degree of icterus. R. Koch has shown that the spirochæta of African relapsing fever is transferred to man by many varieties of ticks, especially the Ornithodorus moubata (Murray), which live in the grasses. European relapsing fever, which differs very little from the African form, is transmitted by bedbugs and perhaps also by fleas and lice. Whether ticks also should be included here is not known. In the African form the ticks transmit the disease to their eggs and so increase their ability as contagion carriers. The disease can be experimentally transmitted to monkeys. The parasites can, under some circumstances, be found even in fresh preparations of the patient's blood. Though it is at times difficult to identify them absolutely because of their brisk movements, this very quality makes their detection easy. The movements consist in a twisting motion around the long axis, lateral motion, and forward motion in the direction of the long axis. Sometimes the unstained spirochætæ are first clearly seen after the movement is somewhat slackened. Examination of stained preparations is easier. The common bacterial stains are suitable, but Giemsa's is the most satisfactory. The usual technic is followed after fixation by alcohol and osmic acid (osmic acid vapor, see below, under Spirochæta pallida). Günther recommends fixing the cover-glass preparations for one hour at a temperature of 75° C., laying them in 5 per cent. acetic acid for five seconds, removing this by washing in water, and passing the cover-glass to and fro over ammonium hydrate solution, and finally staining with gentian violet. Nöggerath's and Stähelin's centrifugalization method (see p. 816) for demonstrating Spirochæta pallida may also be recommended. The Spirochætæ Obermeieri are about 1 μ thick and 10 to 30 μ long. They are usually scanty in the afebrile periods, appear shortly before the onset of the fever, occur in large numbers at the beginning of the fever, and almost or quite disappear again with the crisis. They are found in greatest numbers on the second day of fever. In extravascular blood they are soon clumped (agglutinated) and then destroyed.

[1] Epstein, Amer. Jour. Med. Sci., Sept., 1907, p. 436.

[2] [See, however, the exhaustive studies of Norris, Pappenheimer, and Flournoy (Jour. Infect. Diseases, May, 1906, p. 266), who claim that they must be considered bacteria or, at least, in a class by themselves; and those of Novy and Knapp (ibid., p. 291), who reach the same conclusions.—Ed.]

Spirochæta Pallida of Syphilis (Schaudinn).—One can hardly doubt to-day that the Spirochæta pallida (also termed Treponema pallidum, see Fig. 311), discovered by Schaudinn, is the exciting cause of syphilis. Although this organism is found chiefly in the tissue juices of syphilitic lesions, it has been detected in the blood in the secondary stage of early cases, and even in hereditary syphilis, so that the methods for demonstrating it therein must be considered. Dried preparations are usually employed. They are fixed for one minute in vapor of osmic acid by inverting the slide over a dish filled with the acid, stained in the usual manner with Giemsa's solution for one to two hours (see p. 779), washed, and then examined directly with the oil immersion or first mounted in Canada balsam.

The following methods are also reliable:

Lesser[1] dries the smears in air, fixes them for five minutes in absolute alcohol, and floats the cover-slips for at least an hour on a mixture of 15 drops of Giemsa's solution and 10 cc. distilled water. They are then washed, dried, and examined with the oil-immersion.

Preis[2] fixes by passing the slide three times through the flame, and holds the slide with two clean Cornet forceps. Should the teeth of the forceps be soiled by another dye, the entire preparation is spoiled. He then floods the slide with a mixture of 25 drops of Giemsa's solution in a third of a test-tube full of water, and moves it slowly back and forth about 5 cm. above the flame, until the fluid steams moderately. (It must not boil.) He then washes and repeats the process three or four times with the remainder of the solution. The quicker the procedure, the better does the stain succeed. The stained preparation is then quickly washed in two changes of water and immediately dried with filter-paper. The staining must be such that the

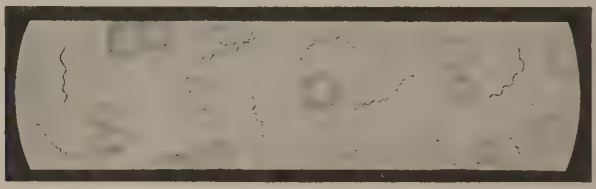


Fig. 311.—Spirochæta pallida or spirochæta of syphilis (after Lesser). One specimen of Spirochæta refringens to the left and one to the right (Schaudinn).

red cells (which appear granular) have the faintest pale pink tinge. If so, the stain is satisfactory and the spirochætæ can be clearly recognized. Otherwise the staining must be repeated on the same preparation.

Nöggerath and Stähelin[3] give the following directions: At least 1 cc. of blood from the lobe of the ear or a vein is dropped into ten times its volume of 0.1 per cent. acetic acid and centrifuged. Smears are made from different layers of the sediment and stained with Giemsa's solution.

Spirochæta pallida is stained a pale pink (therefore, the name pallida), while other spirochætæ assume a bluish tint. It differs from other, saprophytic, spirochætæ, and especially from Spirochæta refringens, which often occurs with it in superficial lesions, by its more numerous and sharper kinks. At either side of Fig. 311 is shown an example of the latter species, which is recognized by its flatter curves, and in stained smears by its different color. Living spirochætæ can be demonstrated in unstained preparations by means of the ultraviolet microscope; indeed, they are easily recognized because of their mobility. The sediment obtained by the Nöggerath-Stähelin method can also be used in the ultraviolet microscope, but, of course, all movement is inhibited by the presence of acetic acid.

THE BLOOD IN MALARIA; MALARIAL PLASMODIA[4]

We owe our knowledge of the malarial parasite, first of all, to the pioneer investigations of the French military surgeon Laveran. Further development in the study of the etiology of malaria has been accomplished chiefly by Italian in-

[1] Lehrbuch der Harn- und Geschlechtskranken, 1906, twelfth ed.
[2] Wien. med. Presse, 1906, No. 49.
[3] Münch. med. Woch., 1905, No. 31, p. 1481.
[4] [The reader is referred to Thayer's Lectures on the Malarial Fevers, Appleton, 1897, and to Deaderick's A Practical Study of Malaria, Saunders, 1909.—Ed.]

vestigators, especially Golgi, Marchiafava, and Celli, and recently by R. Koch and many others. Of the comprehensive articles upon this topic, may be cited the monographs of Mannaberg,[1] which contain what was known to 1899 and numerous original observations. L. Reinhardt's[2] monograph contains a short résumé of the most recent work on the subject.

The knowledge of the most important data concerning the parasites has been obtained from the examination of fresh unstained specimens in which, with the aid of an oil-immersion lens, most of the details described below can be quite easily recognized.

Malarial parasites, ordinarily called plasmodia, are unicellular organisms belonging to the class of sporozoa, subclass hemosporidia, which are on the borderline of the animal and the vegetable kingdoms. They consist of small masses of protoplasm, the diameters of which vary between 1 and 10 μ, according to the age and species of the individuals. The younger specimens are often ring-formed (see Pl. 5, Fig. 3, No. 37), and show active ameboid motion. They develop in the interior of the red blood-cells, destroying their host in their growth. They alter the hemoglobin of the blood-corpuscles which they inhabit to a brownish-black pigment. This pigment is generally visible in the interior of the parasite, undergoing active dancing motion, which may partly depend upon the intrinsic motion of the protoplasm, and should not be confounded with the much slower ameboid motion of the organism. After the parasite has reached a certain stage of development within the red blood-cell, and has more or less completely consumed the latter (Pl. 7, Figs. 1 to 4, 11 to 13, and Pl. 5, Fig. 3, Nos. 36 and 37), it multiplies by merulation (Pl. 7, Figs. 5 to 8 and 16). This takes place by a process of division (see below), varying in the different types, but always in such a manner that nothing remains of the mother organism but the pigment. The free pigment is taken up by the white blood-corpuscles, and, when these are subsequently disintegrated, is deposited in the organs (melanemia). The young parasites produced by subdivision were formerly erroneously known as spores. They differ from the fully developed parasites only in their size, and have none of the characteristics of true spores (Pl. 5, Fig. 3, No. 39, and Pl. 7, 8). They penetrate fresh blood-corpuscles, and then repeat the stages of development. The type of development of the quartan malarial parasite is represented in Plate 7, Figs. 11 to 16; of the tertian organism, in Figs. 1 to 8. The attacks of fever so characteristic of malaria are, generally speaking, associated with merulation of the parasite. These paroxysms follow at regular intervals in the ordinary types of malaria, because the time for the cycle of development of one generation of parasites is a definite quantity which can be usually expressed in terms of days, *e. g.*, tertian and quartan. Types with longer periods (quintan) are more uncommon, and not so thoroughly understood. Most quotidian types, at least in regions where tertian and quartan fever prevail, represent *composite* forms which arise by different generations of tertian or quartan parasites developing in the organism on succeeding days, the one generation being a day older than the other. A quotidian type of fever will be observed if two generations of tertian or three generations of quartan parasites complete their cycle of development on days succeeding each other. This view of quotidian types was prevalent even before the parasite of malaria was discovered, because the attacks were peculiarly grouped together in pairs with reference to their severity and other symptoms (*tertiana duplex, quartiana triplex*). This clinical conception was confirmed by the result of Golgi's study of the parasitic development in the blood. Besides these combined quotidian types, a *true quotidian* type, whose cycle of development lasted only one day, was supposed to exist, until in recent times the investigation of R. Koch[3] (given more in detail below) disproved this idea.

Our knowledge of the morphologic conditions and the development of the malarial parasite is at the present time so complete, thanks to the work of the above-mentioned Italian authors, that a physician familiar with the morphology of the parasites is able, by examining the blood, not only to recognize the presence of malaria, but also to determine the form, type, the clinical course of the attack, and to foretell the time of occurrence of the paroxysms. We shall refer to this later.

Two other kinds of parasites have been observed in the blood in malaria—the so-called *crescents*, of the estivo-autumnal type of the disease, and *flagellate bodies*.

[1] Jul. Mannaberg, Die Malariaparasiten, Wien, 1893, and Malaria volume of Nothnagel's System.

[2] L. Reinhardt, Die Malaria und deren Bekämpfung nach dem Ergebnissen der neusten Forschung, Würzburg, A. Stuber, 1905.

[3] Zeit. f. Hyg., 1899, vol. xxxii.

Figs. 25 to 27, Pl. 7, and No. 38, Fig. 3, Pl. 5 represent types of the crescent series, which are peculiar to the malignant (tropic) form of malaria. They differ in shape from the ordinary plasmodia, and possess a double capsule. The crescents (Figs. 25 to 27, Pl. 7, and Fig. 3, No. 38, Pl. 5) develop in the interior of the red blood-corpuscles, as indicated by the remnant of the adhering hemoglobin margin frequently seen attached to them. Elongated cigar-shaped and spheric formations (ovals and spheres of the crescentic series, Pl. 7, Figs. 25 to 27) develop from the crescents by changes in shape slowly enough to be observed under the microscope. These forms do not possess any ameboid motion proper. Mannaberg (*loc. cit.*) believed that he had proved that the crescents are permanent bodies formed by approximation and fusion of two plasmodia in the interior of the red blood-cells, and that they are therefore a kind of copulation type a so-called syzygy formation. The crescents may divide into their component parts by subsequent segmentation. This idea has not, however, been accepted by other observers. The modern view will be referred to below.

The flagellate bodies are found in all types of malaria (Pl. 7, Figs. 10 and 17). Under the microscope they may be seen to develop from adult plasmodia which have destroyed their blood-corpuscles and have not merulated (Figs. 9 and 15, Pl. 7), and again from the spheres of the crescent series (Figs. 25 and 27, Pl. 7). These flagella suddenly appear at the margin of the parasite; they move very quickly and lash the surrounding blood-corpuscles without, as a rule, inducing active locomotion in the parasite itself. Every once in a while individual flagella will tear themselves off and move about with great rapidity in the field. Their biologic significance will be discussed later.

Unstained blood-preparations may be employed to detect the malarial parasites. They should be especially thin (p. 770 et seq.), so that the individual blood-corpuscles may not overlap nor stick together and form rouleaux. The preparations are best examined with an oil-immersion, Abbé's condenser, and a half-open iris diaphragm. The pigmented forms, the crescents, and the flagellate types can be very easily detected, but the hyaline forms are not so easily differentiated from the endoglobular types of degeneration which are seen in fresh preparations after the lapse of a little time, and which were formerly considered vacuoles. (See p. 782 and Pl. 7, 18 to 22.) Differences of light refraction, however, cause a more sharply outlined contour in the latter than in the plasmodia. Ameboid motion is common to both. (See p. 783.) Doubtful cases can be decided by examining stained preparations (see below). Where so few plasmodia occur as to be difficult to demonstrate, Türk recommends diluting the blood ten times with a ½ per cent. solution of acetic acid, just as for counting plasmodia and leukocytes (see below), and searching for pigmented forms, which are usually quickly found with lower powers of the microscope. The leukocytes and plasmodia will be preserved and the red blood-corpuscles destroyed, or, at any rate, be rendered invisible.

Malarial blood should be stained as indicated on p. 772 et seq. Staining is especially advisable in demonstrating the tropic forms of the parasite, which, on account of their small content of pigment, are often difficult to detect in any other way. Fixation may be accomplished in various ways instead of by heating, by allowing the slides to remain for five minutes in absolute alcohol.

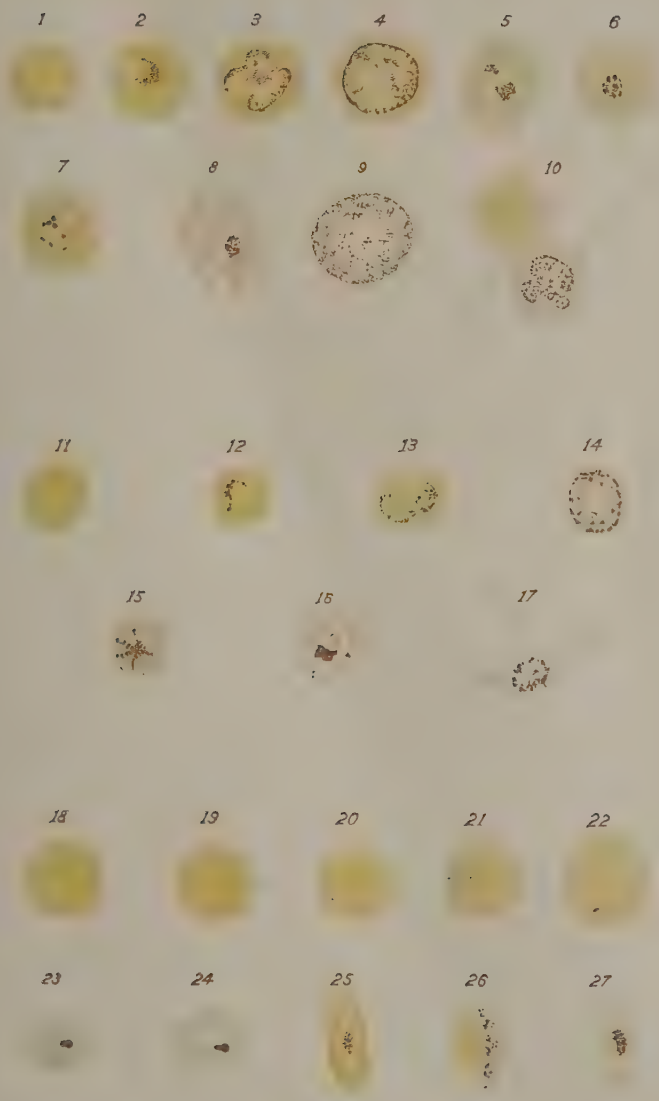
The simplest stain is borax methylene-blue, first recommended by the author, and best employed after Manson's method: 2 gm. methylene-blue are dissolved in 100 cc. of boiling 5 per cent. borax solution. For use this stock solution is diluted in a test-tube with sufficient water to make it just transparent. The preparations are fixed by heat or alcohol for twenty minutes, stained for ten to fifteen seconds, and then washed in water. Ordinary methylene-blue also gives good results.

The endoglobular degeneration spots remain colorless, but the plasmodia stain well with methylene-blue, and show a characteristic structure, namely, an unstained nucleus and sometimes a stained nucleolus. The structure, especially the stained nucleolus, enables us to distinguish blood-plates and granular débris of the blood from the young merulation forms of malarial parasites. The blood-plates show no nucleus and are devoid of structure; the red cells are greenish, and the nuclei of the leukocytes intense blue.

Even Jenner's stain without previous fixation gives good results.

For the recognition of the finer structures of the malarial parasites Mannaberg's, Koch's, and Romanowsky's stains are to be preferred. Nowadays they are always employed according to Giemsa's or Leishman's technic. (See pp. 779, 780 et seq.) With this stain the protoplasm of the parasite appears blue, the chromatin an intense red, the normal elements of the blood as described on p. 779 et seq. The red granule

PLATE 7.



VARIOUS FORMS OF MALARIAL PARASITES (Thayer and Hewetson).

FIGS. 1 to 10 inclusive, tertian organisms; FIGS. 11 to 17 inclusive, quartan organisms; FIGS. 18 to 27 inclusive, estivo-autumnal organisms.

FIG. 1.—Young hyaline form; 2, hyaline form with beginning pigmentation; 3, pigmented form; 4, full-grown pigmented form; 5, 6, 7, 8, segmenting forms; 9, extracellular pigmented form; 10, flagellate form.

FIG. 11.—Young hyaline form; 12, 13, pigmented forms; 14, fully-developed pigmented form; 15, 16, segmenting forms; 17, flagellate form

FIGS. 18, 19, 20.—Ring-like and cross-like hyaline forms; 21, 22, pigmented forms; 23, 24, segmenting forms; 25, 26, 27, crescents.

of chromatin, which is eccentrically placed in the unstained nucleus of the immature ring-form, is particularly characteristic (seal-ring form, Pl. 5, Fig. 3, No. 37). The young merulation forms may be sharply differentiated from platelets by their conspicuous red chromatin granules. (See Pl. 5, Fig. 3, No. 39.)

It should be noted that in stained smears the immature plasmodia which are as yet in the red cells are almost always ring-forms (Pl. 7, Figs. 18 and 20, Pl. 5, Fig 3, No. 37).

To find malarial plasmodia quickly when they are but sparingly present, R. Ruge [1] recommends employing a thick layer of blood from which the hemoglobin has been removed before staining, in a similar manner to the method described upon p. 812. A cover-glass is thickly smeared with blood, dried, and then laid with the smeared surface down in a watch-glass containing 2 per cent. formaldehyd and a ½ to 1 per cent. acetic acid. A few minutes suffice to fix the specimen and also to extract its hemoglobin. It is now stained with methylene-blue in the ordinary manner, and the plasmodia may be readily found, even though there be a number of layers of erythrocytes. This procedure has the advantage of employing more than twenty times the volume of blood utilized in the usual cover-glass smear. Ruge admits, however, that there is always a greater or less amount of precipitate, which an inexperienced observer might differentiate from plasmodia with difficulty. He also calls attention to the fact that the characteristic ring-forms of the young malarial plasmodia (p. 818) are beautifully shown by this procedure.

Counting the plasmodia gives more or less information as to the severity of a malarial infection. Türk counts them in the same way as leukocytes (p. 757 et seq.), in a ½ per cent. solution of acetic acid, a method available only for the pigmented forms. The time of counting should, therefore, be immediately before the paroxysm, *e. g.*, in tertian fever, the evening before the day of fever. Türk's figures vary between 6700 and 16,800 per cubic millimeter.

The *diagnostic significance* of malarial parasites in the blood is absolute. The unmistakable presence of a single parasite is sufficient for a diagnosis of malaria (the pigmented forms and the crescents cannot be mistaken). Negative results are not so certain, because many cases of malaria require a long search before a single parasite is seen. The blood should be examined both during and between the attacks. Even the most expert investigators have been sometimes compelled to make the diagnosis of malaria without finding the parasite. In these cases the parasites are either very few in number or else are supposed to develop in the tissues rather than in the blood. An inexperienced examiner should always mistrust a negative result and repeat his search. In case of repeated negative blood-examination, suspicion should be directed to the presence of one or more diseases, which are easily confounded with malaria clinically, *e. g.*, acute sepsis, irregular cholelithiasis, ulcerative endocarditis, etc.

The blood of severe malaria shows, in addition, the characteristics of anemic blood. The diminution of hemoglobin and of the number of red cells is explained by the destruction of the latter by the parasites. Poikilocytosis is by no means uncommon; even normoblasts and megaloblasts have been observed. There is usually no pronounced permanent leukocytosis, but rather a leukopenia. (See p. 802.) The presence of pigment in the white blood-corpuscles or pigment floating free in the blood is of considerable diagnostic importance if the parasites cannot be found. (See pp. 802 and 811.) The red blood-cells which are invaded by the parasites may be altered in various ways. The ordinary types usually decolorize the cells gradually, until finally all that is left is an indistinct stroma surrounding the parasite. The blood-corpuscles may be considerably enlarged by the tertian parasites, which differ from the quartan variety in this respect (Pl. 7, Figs. 12 to 14). In the malignant types the infected blood-corpuscles shrink and become darker, and, according to Mannaberg, resemble the color of old brass (brassy bodies). In regard to the occurrence of the pernicious anemia blood-picture in malaria, see p. 802.

Differentiation of the Varieties of Plasmodia.—The majority of investigators have concluded that the various forms of malarial parasites found in the blood represent various developmental phases, not only of the same, but also of different, species. Each type of malaria which is characterized clinically and endemiologically represents a separate species of parasites with a definite cycle of development. The reasons for these views may be found in Mannaberg's monograph. He describes the following five species of parasites:

1. The parasites of quartan fever.
2. The parasites of the common tertian fever.

[1] See Mannaberg in Malaria volume of Nothnagel's System.

3. Pigmented quotidian parasites.
4. Non-pigmented quotidian parasites. } Malignant types with crescents.
5. Malignant tertian parasites.

Those of 3, 4, and 5 are malignant varieties with crescents, which probably explains the difficulty with which these cases are influenced by quinin.

R. Koch, on the other hand, considers these three groups of parasites as one species, which is to blame for the malignant summer fevers (estivo-autumnal) of southern Europe, especially of Italy and of the tropics. Koch, therefore, distinguishes only the parasites of *quartan*, *tertian*, and *tropic* fever. He shows that a fresh infection of the parasite of tropic fever always produces attacks of a pronounced tertian type (corresponding to the term 5, malignant tertian parasites). When the disease has persisted for some time and the natural course has been more or less influenced by treatment with quinin, there may develop from the tertian type either a quotidian type, an irregularly remitting, or a continued fever. According to this view there is no true quotidian parasite. Koch's simplified classification is based more or less upon his view that the difference in the pigment which gives rise to the distinction between the so-called pigmented and non-pigmented quotidian parasites (see above) is an artificial condition depending upon the method of preparation. When dry preparations were made skilfully and rapidly, he found that the young parasites of tropic fever were, as a rule, without pigment or had only very fine granules, and, at any rate, were free from clumped pigment, even when the fine pigment lent a brownish diffuse hue; clumped pigment was found only when the parasite underwent subdivision or death. If a wet preparation was allowed to stand for any length of time, clumped pigment was apt to develop. Koch, therefore, maintains that the only correct method of examination is by employing properly dried smears.

For determining the various varieties, Koch lays special stress upon the size of the parasite and the presence of crescents so characteristic of the tropic fevers. The fully developed malignant parasite is barely one-half the size of the tertian or quartan, and it retains the ring-form much longer. Koch makes the following statements in regard to this matter: The young ring-form parasites of tertian and quartan fever have a diameter of about one-quarter to one-third that of the red blood-cells. In size and shape they resemble the fully developed parasite of tropic malaria so completely that they cannot be differentiated. But, as a rule, in tertian and quartan fever, in addition to the small ring-forms, scattered large pigmented parasites are found which may be differentiated from developed malignant parasites by their greater size. If the large mature forms should be absent, the determination of the body temperature at the time of examination will furnish sufficient explanation of the significance of the preparation. If the temperature be low and the paroxysm is over, the parasites must have completed their cycle of development. The small types found must, therefore, represent the fully developed smaller parasites of the tropic malaria. If, on the other hand, the temperature be high and the patient be in the early stages of a paroxysm, then these small ring-forms must be young parasites of the tertian and quartan groups which have not yet reached their full size.

The variations of merulation also serve to distinguish the individual varieties. This is seen in Plate 7 better than it can be described. The regular sun-flower segmentation forms of the quartan (Figs. 5, 6, and 7) may be differentiated from the irregularly segmenting tertian parasites (Fig. 16). Another rather characteristic appearance of the quartan parasite during its development in the afebrile stage is its band-like form stretching from one edge of the red cell to the other.

It is of some clinical interest to be able to predict the time of a paroxysm merely from the period of merulation (Figs. 5 to 8 and 16). It usually takes place three to five hours after the merulation forms have appeared.

The *crescents* are said to be formed in the blood eight days after infection. If these persist in the blood along with the other forms of the parasite, after cessation of fever, recurrences may be expected. There is ordinarily no fever when crescent forms only are present. The significance of the so-called *flagellate forms* has recently been explained.

Sexual Cycles of Development—Significance of the Flagellate Forms and Crescents.—The investigations of Ross, MacCullum, Sakharoff, Koch, *et al.*, with the hemosporidia species halteridium and proteosoma, which occur in birds' blood and which are closely related to the malarial parasites of human blood, have shown that, besides the endogenic cycle of development culminating in merulation, there is a second sexual cycle of development. Koch divides this into the following stages: 1. Separation of the parasite from the red blood-corpuscle. Differentiation into

male and female elements. The male gametes (microgametes) differ from the female gametes (macrogametes) by their greater chromatin content and usually by their smaller size. The thread-like formations which were formerly considered flagella develop from the interior of the male. They separate, propel themselves independently, and play the part of spermatozoa. 2. Fecundation by penetration of the spermatozoa into the female plasmodia. This takes place in the stomach of a mosquito (intermediate host) which has sucked the blood from some infected bird. 3. Change of the impregnated female parasites into worm-shaped bodies. 4. Penetration of the stomach-wall of the mosquito by the latter and their change to coccidia-like spheres. 5. Formation of sickle-shaped bodies (spores) in these spheres. 6. Deposit of these, fully developed and liberated, in the veneno-salivary glands and perhaps in the other organs of the mosquito. 7. Transmission of young parasites again to birds by fresh bites of the mosquito.

It has been shown that these biologic facts are also true for the parasites of human malaria, especially since the transmission of the disease by mosquito bites, an old and popular belief, has recently been definitely proved experimentally.

It may, at the present time, be considered proved that the crescents represent simply the first stage of the gametes (macro- and microgametes, *i. e.*, female and male forms of the tropical estivo-autumnal), malarial parasite. These in the course of development lose their double form, assume an oval and then a spheric shape, and from this moment are divided into male and female gametes (micro- and macrogametes). The male gametes of this form put forth flagella-like spermatozoa analogous to the gametes of the non-tropical forms. Whether or not, in spite of this conception of the insignificance of the crescents, Mannaberg's view of their origin (see above) is correct is yet undecided. The two theories are not absolutely inconsistent.

It is of considerable pathologic interest to know that the action of quinin results in necrosis of the parasite. This may be recognized in stained preparations by the disappearance of the nucleus. Very young parasites are more susceptible to its action, which accounts for the rule that it is best to give quinin three or four hours before an attack is expected. The crescents are almost immune to the direct action of quinin, as shown by microscopic examination, so that the action of repeated doses of quinin in malignant types resembles more or less a process of fractional sterilization. The crescents themselves are not disturbed, but the plasmodia developing from them are killed by the repeated doses. In exceptional cases, however, the crescents are not so resistant.

TRYPANOSOMES IN THE BLOOD

The human trypanosome diseases which have only recently been exhaustively studied are becoming of greater practical importance on account of their increasing spread throughout Africa. They arise from an infection of the body, and especially the blood, by the Trypanosoma Gambiensi, a protozoön belonging to the group Flagellata or Mastigophora. (See Fig. 312.) The trypanosome is spindle-shaped, with a rounded anterior and a tapering posterior extremity. In the granular protoplasm are a rather large nucleus and a vacuole, the latter at the forward end. A long flagellum which arises from a collection of chromatin at the forward end of the cell turns backward in the direction of the cell-body, with which it is connected by a so-called undulating membrane, and at the hinder end forms a free thread. By Giemsa's stain, the flagellum (including the edge of the undulating membrane), the nucleus, and the collection of chromatin at the anterior end are colored red while the remaining parts are a violet blue. The parasites can be recognized even in fresh preparations if pressure on the cover-slip be avoided (for they are very fragile). To do so it is best to rim the cover-slip with a thin layer of paraffin. In such preparations the parasites move in odd spiral paths among the red cells, to which they impart very slight motion. They can be recognized by low-power lenses since they are

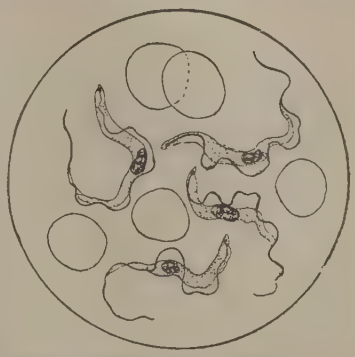


Fig. 312.—Trypanosoma Gambiensi in the blood (after Guiart and Grimbert).

15 to 30 μ long (3 to 6 times as long as a red cell) and 1.4 to 2.5 μ broad. The smears must be made very thin, and very gently. The use of a little piece of gold-beater's skin held in a pair of forceps is recommended for making the smears. The slide method may also be recommended as very satisfactory. Stäubli's sedimentation method for demonstrating trichina embryos in the blood (see p. 823) may be mentioned in this connection. The vapor from a mixture of osmic and acetic acids is recommended for fixation, but immersion in a mixture of 10 parts of commercial formalin and 90 parts of absolute alcohol gives good results. Giemsa's and Leishman's stains are best. (See p. 779 et seq.) Besides the perfect organisms, degeneration forms are also found. These are ameboid, pear-shaped, or spheric structures without flagella. The parasites are sometimes present in the blood in very small numbers and may even disappear from it, so that occasionally puncture of the cervical lymph-nodes, in the tissue juices of which they are numerous, is necessary. They may disappear from the blood for long periods and then reappear in great numbers. Guiart and Grimbert[1] recommend making smears from the upper layers of the sediment obtained by mixing the blood with a 1 per cent. solution of sodium citrate (to prevent coagulation) and centrifuging repeatedly. Possibly the Stähelin-Nöggerath method, used to demonstrate spirochætæ, could be used in searching for trypanosomes. The parasites would then be concentrated in a small amount of plasma. In severe cases the organisms are found in the cerebrospinal fluid as well as in the blood and lymph-nodes. Trypanosomiasis runs a chronic course, with an irregular fever, cachexia, localized edema of the face, trunk, and legs, and enlargement of the lymph-nodes and spleen. The special form, called *sleeping sickness*, which cannot be differentiated etiologically from the others, seems to be in some way connected with the presence of trypanosomes (frequently together with streptococci) in the cerebrospinal fluid. The sleeping sickness is to some extent the terminal stage of trypanosomiasis. The parasites are carried by a kind of biting fly, Glossina palpalis. Trypanosoma Gambiensis, the variety occurring in man, can hardly be distinguished from certain other varieties observed in animals. It belongs, according to Koch, to a group of trypanosomes which have not phylogenetically been divided into definite species, and which vary in virulence and morphology in different hosts, Several different varieties occur in man as well as in animals. The species occurring in man cannot be sharply differentiated from those of the tsetse disease (nagaña) of horses and cattle in Africa. There is, however, a group of distinct species which Koch calls permanent varieties and which have a strong affinity for particular animals, but which do not occur in man. To these species belong the trypanosomes found in rats; those of surra of horses, asses, and camels, in India and the Philippines; those of Mal de Caderas of the Equidæ of South America; and those of the dourine of the horse in Algiers, North America, and the valley of the Danube. (For an exhaustive discussion of trypanosomes see Koch, Deut. med. Woch., 1904, No. 47, and for a more recent review of the forms occurring in man see Martin Meyers, Ergebn. d. inn. Med., und Kinderheilk., 1908, vol. ii.)

PIROPLASMATA IN THE BLOOD

The piroplasmata are peculiar protozoöns which owe their name to the pear shape of certain of their developmental forms. As parasites of the red cells of many animals, they play an important rôle. They are the cause of Texas fever (transmitted by ticks) and of the coast fever of cattle as well as other important animal diseases of tropic and subtropic countries. Neither their presence in human blood nor their significance as a cause of disease in man has been demonstrated. Purple fever, a peculiar disease endemic in the Rocky Mountains, was formerly ascribed to piroplasmata, but more recent researches point to a spirocheta as the cause. A febrile disease, called tropic splenomegaly, first described by Leishman in India, but also observed in China and Japan, was thought to be due to a kind of piroplasma, the Leishman-Donovan bodies. Recent studies of Kossel, Weber, Schaudinn, and Rogers have shown that this is a pear-shaped descendant of the trypanosome. Until further evidence comes to hand piroplasmata should not be regarded as human parasites.

WORM EMBRYOS IN THE BLOOD

Filaria and Trichina

Of the two helminthes inhabiting the human blood in the tropics, Distomum hæmatobium (Bilharzia hæmatobia) and Filaria sanguinis, only the latter is of

[1] Diagnostic chimique microscopique, etc., Paris, 1906.

diagnostic importance in blood-examinations. The blood of patients infected with filaria (tropic chyluria) contains numerous small, thread-like worms, the filaria embryos, 0.21 to 0.36 mm. long and 0.004 to 0.0075 mm. broad (Figs. 313 and 272, p. 694). For the other blood-findings, see p. 840. Recently different varieties of Filaria sanguinis have been distinguished, of which Filaria Bancrofti (nocturna) is the most frequent (Fig. 313). This organism appears in the blood only at night. Filaria diurna, whose embryo appears only in the daytime, and Filaria perstans, whose embryos are present day and night, have been described. In addition, Filaria gigas, Filaria Demarquai, Filaria Megalhäesi, Filaria loa and Filaria Ozzardi may be mentioned.

Fig. 313.—Filaria Bancrofti (nocturna) (after Emerson).

According to Stäubli's experimental studies, the demonstration of trichina embryos in the blood will have to be considered in the diagnosis of *trichinosis* in the future, although to the best of the author's knowledge they have not yet been demonstrated in man. [Herrick and Janeway[1] and Mercur and Barrach[2] report the demonstration of trichina embryos in two cases; 10 cc. of blood were withdrawn from a vein in the arm and Stäubli's method (see below) was used in both instances. The organisms were found in the fresh sediment. All stained smears, however, proved negative.—Ed.] Stäubli found the trichina embryos in the blood of guinea-pigs seven days after the ingestion of infected meat. He used the following method of examination: All the blood that can be obtained from the animal's heart[3] is immediately mixed with a large volume (20 to 30 cc.) of 3 per cent. acetic acid. This destroys the red cells without injuring the parasites. The mixture is centrifuged and examined with the low power (Zeiss A with ocular No. 3), either directly or after staining smears dried by gentle heat. Jenner's stain is satisfactory. The embryos stain an intense blue with a pale red border. They are about 0.08 mm. long and not quite so thick as the diameter of a red cell. (See Fig. 224 *c*, p. 524.) Stäubli thinks that this method can be used in demonstrating any parasites in the blood (Filaria, Trypanosoma, etc.). Indeed, Nöggerath and Stähelin have used a modified form of it to demonstrate Spirochæta pallida. (See p. 816.) Stäubli pictures a low magnification of a smear obtained by this method.

CONDITION OF THE BLOOD IN THE MOST IMPORTANT BLOOD-DISEASES

THE ANEMIAS

The condition ordinarily called *anemia* should more correctly be termed *oligochromemia*. Either merely the quantity of hemoglobin in the blood may be decreased, or the number of erythrocytes may also be simultaneously diminished. Such differences in the individual anemias are shown by the magnitude of the hemoglobin quotient or color index. (See p. 765 et seq.) In anemia from hemorrhage and sometimes, according to recent researches (see p. 734), even in pernicious anemia, there is, on the contrary, a diminution in the mass of blood. In the former case this is, however, only temporary. In all anemias undeveloped (nucleated) erythrocytes may be present in the blood, as the result either of a disturbed or of an incomplete development. The subdivisions of anemia vary considerably. The following arrangement would seem to correspond best to the actual conditions.

The previously accepted division of anemias into primary and secondary is no longer possible, for a constantly increasing number of so-called primary anemias, to which pernicious anemia belongs, are being proved to be secondary. The conception of a primary disease is highly unscientific, for even the so-called primary diseases are the consequence of some preëxisting cause, which we either do not know or illogically ignore in our terminology. In regard to anemia in infectious diseases, see p. 798.

[1] Archives of Int. Med., 1909, vol. iii, p. 263.

[2] Ibid., 1910, vol. v, p. 530.

[3] It has yet to be proved whether or not venous blood, which must be used in man, is satisfactory, since it is quite conceivable that the embryos do not pass into the general circulation, but immediately collect in the muscles. (See Ed. note above.)

Chlorosis.—The chief characteristic of the blood in chlorosis is a diminution in the amount of hemoglobin. This is not infrequently as low as 20 or even 15 per cent. According to Plesch and Oerum,[1] the mass of blood seems usually to be increased. Though there may be a normal red cell count, the number of red blood-corpuscles is also usually diminished, and sometimes very considerably (1,500,000); but it is more or less characteristic that the diminution of hemoglobin in chlorosis is more marked than the diminution of the number of red cells.

The *color index* (hemoglobin quotient or value, p. 765 et seq.) is therefore less than 1. The pallor of an individual blood-corpuscle may sometimes be recognized microscopically. (See p. 783.) In chlorosis the volume index (volume quotient) is usually diminished (see p. 785 et seq.) approximately in proportion to the severity of the disease. The individual red cells vary in size. The number of small forms varies with the volume index. However, occasionally abnormally large cells are found which differ from megalocytes of pernicious anemia by their less intense stain. (See p. 785.) Severe cases of chlorosis exhibit poikilocytes, microcytes, nucleated red cells (normoblasts and even, in the most severe cases, megaloblasts), and the degenerated forms of red blood-cells described by Maragliano (p. 782 and Pl. 7, 24 to 28). Granular basophilic and polychromatophilic changes in the erythrocytes may be present. (See p. 784 et seq.) The number of white corpuscles and of blood-platelets is usually within normal figures. Muir, as well as Hanot and Matthieux, found an increase in the blood-platelets (350,000 to 400,000). This coincides with the tendency of chlorotic patients to the formation of thrombi. The differential count of the leukocytes is normal. During convalescence Nägeli found a high leukocyte count with an increase in the eosinophiles. Neusser considers such an increase of favorable prognosis. A diagnosis of chlorosis cannot always be made from an examination of the blood alone, as in many cases it depends considerably upon the clinical picture. Chlorosis is a disease occurring during the period of development, especially in women, and is probably to be explained by the fact that the amount of blood formed is not sufficient for the demands of the growing organism.[2]

The urine of chlorotics is pale and contains but little urobilin. This favors the theory just given, and indicates that the destruction of red blood-corpuscles is limited, for in some other types of anemia, especially in so-called *pernicious anemia*, the increased destruction of red cells is manifested clinically in a dark urine, which contains a good deal of urobilin. The patient is usually well nourished, and may even be increased in weight, and this is responsible for the peculiar appearance of many cases of chlorosis. Von Noorden demonstrated that this abundance of fat in chlorotics is not due to the diminution of the oxygen content of the organism from deficiency in the hemoglobin of the blood, but to the relatively diminished exercise enforced upon the patient by the disease.

The following remarks refer to the clinical picture which the author has termed *masked* (*larval*) chlorosis.[3] The consideration of this as a clinical entity is based

[1] Pelsch, Cong. f. inn. Med., 1907, reference in Berlin. klin. Woch., 1907, No. 23, p. 731; Oerum, Arch. f. klin. Med., 1908, vol. xciii, p. 4.

[2] The question whether chlorosis occurs in males also is, of course, pertinent only if the condition "of the female sex" be omitted from the definition. The extraordinary preponderance of females suffering from this disorder during puberty argues for the separation of the disease from analogous anemias in males, and for the theory that chlorosis is in some measure a secondary pathologic condition of the female sex. It must be associated with the peculiarities of the female sex. Apparently, disturbances somewhere in the generative organs inhibit the stimuli which affect the blood-forming organs, upon which is dependent the normal blood-formation of the female. The conception that blood-formation is intimately connected with the female sexual organs has much in its favor, as it is reasonable to assume that the female body, which loses blood during menstruation, a process peculiar to the sex, must have an adaptive mechanism in the genitalia which serves to stimulate blood-formation. The supposition also explains how even later, after development is complete, conditions may arise which in all respects except the age of the patients correspond to chlorosis and indeed are frequently to be regarded (exclusive of recrudescence of chlorosis) as disturbances of genital functions. In such a patient the history of a previous chlorosis in youth frequently argues for such an assumption, as does also the introduction of the relapse by amenorrhea, just as is observed at the onset of chlorosis.

[3] See Dubnikoff, Klinische Untersuchung über Eisenwirkung und larvierte Chlorosis, I. A. D., Bern, 1908, and Seiler, Ueber larvierte Chlorosis, Correspondenzbl. f. Schw. Aerzte, 1908.

upon the fact that there are patients who suffer from the general symptoms of chlorosis in whom the hemoglobin percentage is either normal or only slightly below normal. Thus the hemoglobin may be 88 to 94 per cent. (corrected),[1] which, although found in normal individuals, is to be considered an abnormally low value in the patient, since the administration of iron influences the general symptoms favorably and increases the hemoglobin. On the other hand, there are patients with the same hemoglobin percentage and other symptoms of chlorosis who do not react at all to iron, and in whom, as a rule, further observation and study lead to the diagnosis of another malady, especially incipient tuberculosis or neurasthenia. It follows from this that in these cases the study of the blood alone does not establish the diagnosis of chlorosis, but that besides excluding other diseases, it is necessary to make the therapeutic test. The author would discourage the tendency to regard hemoglobin estimations as superfluous and would advise against the administration of iron in all pale patients, since only a small minority of the patients without a marked decrease in hemoglobin derive any benefit from iron, and by the use of hemoglobin estimations, one has a far surer basis for his therapy than without.

This conception of masked chlorosis advanced by the author should not be confused with that of pseudochlorosis advanced by Laache, to which it is in a way opposed. In contrasting such cases with chlorosis Laache has in mind anemic looking men, in whom the pallor is caused by "previous processes which cannot be more accurately designated" without any change in the hemoglobin percentage The name pseudochlorosis was suggested to him by the name pseudoanæmia spastica, applied to angiospastic conditions. Nor is masked chlorosis to be identified with the pseudoanemia of Strauss [2] since he includes the pallor of perfectly healthy as well as that of really sick individuals in whom there is no diminution of hemoglobin. In opposition to these ideas of pseudochlorosis and pseudoanemia the author would emphasize that masked chlorosis, though difficult to diagnose, is an actual clinical entity and in no sense a false chlorosis.

Simple So-called Primary Anemia.—Under this term we may include all cases except *chlorosis* and so-called *pernicious anemia*, where there is a diminution of the hemoglobin or red cells, either of one or both at the same time, and where no other disease is present which can cause the conditions. Simple primary anemia, like chlorosis, can be considered a disease of the blood-forming organs; it differs from chlorosis only in that it does not affect growing individuals, and is not, therefore, a disease of development. The fact that the condition of the blood in simple primary anemia is identical with that of chlorosis supports this view.

The so-called *masculine chlorosis* of males during puberty may well belong to this group. The much greater frequency of chlorosis in women argues for a separation of these cases from chlorosis proper (see p. 824), for it shows that the latter is, to a certain degree, a pathologic sexual characteristic peculiar to females. The fact that the simple so-called primary anemias of males are not connected with puberty to the same degree as is chlorosis, and that they cannot therefore be considered peculiar to this period of life, is a further argument for the separation.

Infantile Pseudoleukemic Anemia (v. Jaksch-Hayem).—This term is applied to a peculiar anemia, sometimes congenital, but usually occurring in earliest infancy, frequently, indeed, in the first month and persisting through the first year. It resembles true pernicious anemia in that megalocytes and megaloblasts are found, but differs from it in the occurrence of a leukocytosis, partly polynuclear, partly lymphocytic. It has no definite etiology. The cause has been ascribed to digestive disturbances, rachitis, syphilis, and other diseases. The red cells may be reduced to 1,000,000; the hemoglobin, to 20 per cent. The color-index may be greater or less than 1. Megalocytes, microcytes, poikilocytosis, anisocytosis, polychromatophilia, and basophilic degeneration of the red cells may be found. Megaloblasts and normoblasts are present, the latter usually in great numbers. The leukocytosis may reach 20,000 or more. It is in most cases decidedly polyneutrophilic; in others, on the contrary, it is a pure lymphocytosis. At times myelocytes are found in great numbers, so that confusion with myeloid leukemia is conceivable, although the latter never, or at any rate very rarely, occurs at this age. (See p. 835 et seq.) The eosinophiles may be either increased or decreased in numbers. The spleen is usually large. The bone-marrow is dark red.[3]

[1] In regard to the meaning of corrected percentages see p. 753.

[2] Berlin. klin. Woch., 1907, No. 19.

[3] For the pathologic anatomy see Nägeli, Blutkrankheiten und Blutdiagnostik, p. 293, et seq.

Besides the cases presenting the above typical clinical picture, many cases of secondary anemia occur which resemble infantile pseudoleukemic anemia more or less closely. It is, therefore, quite right to consider these peculiar symptoms of infantile anemias (especially the tendency to leukocytosis) as the expression of the peculiar reactive ability of the immature blood-forming organs and not of a specific disease.

So-called Pernicious Anemia (see Pl. 7, Fig. 1).—As indicated by its name, this disease is malignant, and implies an unfavorable prognosis. This view, however, does not entirely explain the situation, for the severity of the symptoms is a relative affair, and undoubtedly many cases of so-called pernicious anemia have recovered. Only the so-called idiopathic or cryptogenetic (Biermer) form of pernicious anemia is truly incurable; yet even this form does not differ sharply either in the blood-picture or (at least according to the author's theory, introduced below) even in the etiology from cases where pernicious anemia is secondary to a curable malady. The characteristic of incurability alone is not sufficient to differentiate it from other anemias which may also be incurable. Indeed, it would be more suitable to seek for the essential differences between pernicious anemia and chlorosis or the so-called simple anemias not only in signs of defective blood formation, but also in those of abnormal destruction of blood-corpuscles, which latter does not concern these other anemias. The only sharp definition of pernicious anemia (in which, as we express it, the bone-marrow reverts to the embryonic type) is based on the changes in the morphology of the blood. The special features are the occurrence of megalocytes, the high color-index, and, in the majority of cases, the appearances of megaloblasts. The destructibility of red blood-corpuscles in pernicious anemia is usually indicated clinically by the marked poikilocytosis, the presence of basophilic degeneration of the red cells, and the presence of urobilinuria and icterus. Anatomically, there is a deposit of iron in the liver and kidneys, as shown by Quincke. The basophilic stippling and the polychromatophilic changes in the red cells (see p. 783 et seq.) which occur so frequently in this disease should no longer, as formerly, be considered degenerative, but rather regenerative, changes. For a definition of the disease see Nageli's excellent review (Blutkrankheiten und Blutdiagnostik, 1908, p. 252).

The number of red cells is usually considerably more diminished in pernicious anemia than in chlorosis and simple primary anemia, and sometimes to a very marked degree. In a case of Quincke's the red cell count was 143,000 per c.mm. This diminution is generally more marked than the reduction of the hemoglobin, hence the color-index is above 1. This is chiefly due to the preponderance of abnormally large erythrocytes, as is expressed by the volume index (see p. 785), and is evident in the stained smears. In addition, at least a part of the smaller red cells are evidently abnormally rich in hemoglobin. (See, however, Capp's assertion, p. 786, that the red cells are normally saturated with hemoglobin.) The corrected hemoglobin percentage must be used in determining the color-index (p. 753 et seq.).

The macrocytes, so characteristic of pernicious anemia, may measure 12 μ or more in diameter. Normal sized red cells, moderately enlarged megalocytes, and microcytes are included. Microcytes are, however, less characteristic than megalocytes. Abnormally pale as well as abnormally red cells are present. It is usually possible to find stippled cells (erythrocytes with basophile granules), although in very small numbers; and red cells with polychromatophilic changes are more or less abundant. The presence of megaloblasts in the blood, however, is specially characteristic of pernicious anemia. They are usually very scanty and require patient searching. They are found only exceptionally in large numbers, and then only in the agony of death.

They may be absent for long periods. They sometimes show destruction of the nucleus, and rarely mitoses. The author has frequently observed the development of megaloblasts, as the lesion in the blood became more severe, after a positive diagnosis of pernicious anemia had been made from the other symptoms. The presence of megaloblasts should not, therefore, be considered absolutely necessary for the establishment of a diagnosis; indeed, megaloblasts are lacking in the most severe form (the so-called *aplastic* pernicious anemia, see below), in which the bone-marrow remains yellow in color and shows no sign of regeneration. This, however, is in itself by no means diagnostic of the aplastic nature of the disease. Much more suggestive of this condition are a very marked leukopenia and other evidences of a lack of regenerative power, such as the absence of polychromatophilia, of basophile degeneration, and of normoblasts. In certain stages of pernicious anemia the latter occur in great numbers either alone or together with megaloblasts. During periods of improvement the megaloblasts are usually reduced in numbers and may be more or less completely replaced by normoblasts. During the temporary arrest of idiopathic

pernicious anemia effected by arsenic, all nucleated red cells gradually disappear. The same is true of the complete cure of certain other forms.

The number of leukocytes is usually diminished in pernicious anemia. As the function of the bone-marrow is diminished, this decrease is at the expense of the polynuclear leukocytes, so that the lymphocytes seem to be relatively increased. According to Ehrlich and Lazarus, they may constitute 62 per cent. of the total number. Strauss [1] regards the decrea.e of the polynuclear leukocytes as characteristic of true pernicious anemia, as compared with anemia following carcinoma, in which the percentage of the polynuclear cells is usually greater than that of the mononuclear, and in which there is frequently present a pronounced polynuclear leukocytosis. The latter peculiarity, however, is not always present in the anemia of carcinoma, and may sometimes be observed during a temporary improvement in pernicious anemia. In pernicious anemia the blood-plates are diminished in number.

The ordinary form of pernicious anemia is characterized by a peculiar reaction of the bone-marrow, manifested by a replacement of the fatty by a red marrow and by the embryonic type of blood-formation which, according to Nägeli, include the megalocytes, the high color-index, and the megaloblasts. Yet other cases occur in which this change from a fatty to an active marrow and the blood-picture resulting therefrom are lacking. These cases have been termed *aplastic pernicious anemia*. The aplasia can sometimes be recognized from the blood-picture by the absence of megaloblasts and normoblasts, the absence of polychromatophilia and basophile stippling of the red cells, sometimes by the absence of megalocytes and, finally, by an extraordinary decrease in the number of leukocytes. But, as stated above, the absence of megaloblasts alone is not sufficient to establish the aplastic character of the anemia.

The old supposition that the mass of blood is diminished in pernicious anemia, which was based on postmortem examination, has recently been confirmed by Kottmann's[2] direct estimations of the quantity of blood in the living subject. There are, however, clinical grounds for assuming that in some cases the disease may be complicated by hydremic plethora. Cases of the former class are apparently characterized by a recession of the hemic murmurs (since, owing to the smaller volume of blood, the current is slowed) and by the absence of marked cardiac dilatation; while those of the latter present signs of cardiac enlargement, loud hemic murmurs, venous hums, and frequently distention of the neck veins and subcutaneous edema.

Occurrence and Etiology of Pernicious Anemia.—After Biermer's[3] original description of pernicious anemia and Quincke's[4] exhaustive studies there was a tendency to regard this malady as an etiologic as well as a symptomatic entity. Recent studies, however, have shown that though, corresponding to Biermer's description, the disease, which can be defined to-day only by the blood morphology, may be apparently idiopathic or cryptogenetic, *i. e.*, not preceded by any striking primary illness, and may occur to a certain degree as a specific disease; yet in many cases it has the character of a secondary malady. In the author's opinion the conclusive logical consequence of this fact is that pernicious anemia may, as yet, be considered only a symptom-complex. In his opinion the so-called cryptogenetic or idiopathic cases, and many, perhaps all, of the cases which are considered secondary, have a common and manifest pathogenesis in gastric achylia or marked hypochlorhydria, so that even the idiopathic cases should no longer be considered cryptogenetic. To support this theory, it is necessary to call to mind the occurrence of blood changes resembling those of pernicious anemia in diseases which are manifestly primary. The longest known is the so-called bothriocephalus anemia, which may be classed with analogous anemias due to Tænia mediocanellata and Trichocephalus dispar. Ankylostoma anemia seems to be due essentially to hemorrhage and does not belong to this group. The typical blood-picture of pernicious anemia (showing leukopenia, megaloblasts, and other evidences of the embryonic type of blood-formation) does occur, although rarely, in individual cases of gastric carcinoma, although it must, of course, be granted that in the *majority* of cases of the latter disease, even if megaloblasts be present, the blood-picture differs from that of pernicious anemia in the occurrence of leukocytosis. Nägeli has found the practically typical picture of pernicious anemia in

[1] Strauss and Rohnstein, Die Blutzusammensetzung in den verschiedenen Anämien, Berlin, 1901.

[2] Kottmann, Ueber die Viscosität des Blutes, Correspondenzbl. f. Schweiz. Aerzte, 1907, No. 4.

[3] Correspondenzbl. f. Schweiz. Aerzte, 1872, No. 1.

[4] Deut. Arch. f. klin. Med., vol. xx, xxv, and xxvii.

the puerperium, so that Biermer's old idea of cryptogenicity is no longer tenable in many cases. Nägeli vouches for the occurrence of true pernicious anemia in syphilis, and the author has himself seen such a case to which no objection could be taken. In advanced malarial cachexia and in severe cases of sepsis the blood is sometimes typical of pernicious anemia. On the other hand, the assumption that the characteristic blood-picture may occur from repeated hemorrhages, from malnutrition, and in the terminal stages of severe and protracted chlorosis should be discredited. The alleged occurrence of pernicious anemia resulting from chronic nephritis (French writers) is more likely a combination of two independent diseases. The diseases in which, on account of the more or less close resemblance of the blood-pictures to pernicious anemia, were formerly confused with it will be treated hereafter under differential diagnosis. Aside from the true or cryptogenetic pernicious anemia, the occurrence of the *typical* blood-pictures is limited to certain cases of syphilis, malaria, and intestinal parasites, to the puerperium, and to rare cases of gastric carcinoma and sepsis. Precisely in the most frequent and best known of these conditions, viz., the true or so-called cryptogenetic form, in the bothriocephalus anemia, and in the anemia due to certain gastric carcinomata is there a marked disturbance of the gastric chemistry, evidenced by more or less complete achylia. Older observers were struck by this, and to the author it seems important in explaining the condition and by no means accidental. Unfortunately, nothing certain is known about the gastric chemistry of the other forms. But since the secretion of hydrochloric acid is of such great importance in digestion, it is quite fair to assume that a disturbance of the same has some bearing on the etiology of pernicious anemia. If further study of the remaining cases shows that they are not connected with this functional gastric disturbance, other causes must be found for them. It has been suspected that the general nutritional disturbance depending upon the deranged digestion might give rise to the anemia, but the association of cause and effect was sought in the wrong direction. In order to make this theory harmonize with the facts that gastrectomy has no such effect, and that achylia has been observed without pernicious anemia, it was assumed that the accompanying atrophy of the intestinal mucosa, which was found at autopsy, was the essential cause, because no compensation was made for the gastric disturbance. But, aside from the fact that this finding was soon recognized as a postmortem change, such an explanation is inadmissible, because malnutrition is not known to cause pernicious anemia. There are many severe nutritional disturbances in which pernicious anemia never occurs; and, as a rule, the nutrition of patients with pernicious anemia is maintained for a long time. It was then thought that abnormal decomposition products were formed in the intestine, because of the lack of the HCl secretion, which products, through their toxicity, gave rise to pernicious anemia. But this supposition is purely hypothetic. After these attempts at explanation failed, the whole theory of the absence of HCl as a cause of pernicious anemia was rejected by most writers; or at best was kept in the background, but the simplest explanation of all did not occur to any one. It was thought that bothriocephalus anemia, least of all, could be explained by the theory, since studies of Shapiro[1] and Tallquist[2] had shown that the parasite excretes hemolytic substances which, of course, seemed at first glance to offer sufficient explanation for the anemia. So it came about that the noteworthy discovery of the lack of the hydrochloric acid secretion in the stomach was regarded merely as a concomitant symptom or a consequence of pernicious anemia and of no etiologic significance. The author's argument favoring the significance of the suppression of the acid secretion as a cause is as follows:

As a result of his studies on the therapeutic effect of iron, Quincke [3] demonstrated that iron preparations given to animals are absorbed from the duodenum only, *i. e.*, exactly from the place where the intestinal contents are under the influence of the HCl of the gastric juice. He showed that iron could be easily demonstrated microchemically in the intestinal epithelium. The acid of the gastric juice manifestly serves to dissolve iron salts and hold them in solution. These, through the alkaline action of the bile and the pancreatic juice, are more or less completely precipitated. Quincke's studies seem to show that this is also true of iron in the food, for he found the reaction for iron in the duodenal mucosa after the ingestion of ordinary food. It may, of course, be objected to the supposition that the HCl of the gastric juice plays a part in the absorption of organic iron in the food, that this iron, which is almost all in combination with albumin, is either soluble in non-acid material or at least remains in solution. But, according to the recent physiologic studies of Abderhalden and Cohnheim, the albumin compounds are

[1] Zeit. f. klin. Med., 1888. [2] Ibid., 1907, vol. lxi.

[3] Cong. f. inn. Med., 1896, p. 290.

much more completely broken up in the stomach than was formerly supposed. In the intestine the cleavage is carried on still further. The author would recall in this connection the work of Cohnheim, who has shown that, under the combined influence of trypsin and erepsin, protein in the intestine is completely broken up to its end-products, *i. e.*, into amino-acids and bases. There can be no doubt that, in the course of this complete decomposition, iron is set free in the intestine and even in the stomach in its so-called inorganic form; and in the absorption, free hydrochloric is surely an important factor. The HCl, in so far as it is not neutralized by the bile and pancreatic juice, is of considerable importance in the duodenum. Even after neutralization of the HCl from the stomach, the intestinal contents has normally certain acid properties; whether one assumes, as do Macfadyen and Nencki as well as Ogata, that the intestinal contents give a distinct acid reaction, or admits, as does Matthes, a reaction alkaline to litmus and acid to phenolphthalein, corresponding to a solution of sodium bicarbonate containing free CO_2. In this reaction there is an acid element present in the form of free carbonic acid, which is capable of holding iron salts in solution. We know that this is true because of the iron content of alkaline chalybeate waters and acid salts. The objection that the decomposition of protein is complete only in the lower bowel through the action of erepsin is not sufficient to belittle the importance of HCl for the absorption of iron, since, as Abderhalden[1] has shown, a large part of the albumin is broken up in the stomach into polypeptone, and even in the lower bowel, where the decomposition of protein is surely complete, a deficit in HCl must make itself felt, in that bicarbonate will be more or less changed into monocarbonate.

It seems to the author that the most probable explanation of pernicious anemia, in cases where the suppression of the HCl secretion is demonstrated, consists simply in the disturbance of iron absorption, since in these cases not only does the organism receive insufficient material for blood-formation, but the bone-marrow lacks the physiologic stimulus to the same. The blood-picture in pernicious anemia indicates, therefore, the reaction of the bone-marrow to an insufficient supply of iron for the needs of the intermediate metabolism. The circumstance that plentiful supplies of iron are found in the deposits of hemosiderin in the livers and kidneys of patients dead of pernicious anemia is not inconsistent with this theory, because, apparently, an increased destruction of badly formed red cells is the cause of this phenomenon, and because it is quite conceivable that if the stimulation of the bone-marrow be lacking, owing to the failure of iron absorption, the organism is no longer able to make use of these deposits formed from the destruction of the red cells.

The peculiar reversion of the bone-marrow to the embryonic type of blood-formation, so often emphasized, argues for this theory of pernicious anemia, for the embryo must behave as the patient with achylia, in so far as it does without the stimulus afforded by the absorption of iron. The facts that, as a rule, no benefit results from the administration of iron alone, and that, as the author has often seen, a combination of iron and large amounts of acid often succeeds, are also in accord with the theory. In the former iron is not absorbed in sufficient quantity, owing to the lack of acid. Organic acids, especially lactic acid, which are afterward oxidized in the body are adapted to this purpose, but not HCl (combination of iron with kefir cure). The theory is further supported by the fact that cases of so-called cryptogenetic pernicious anemia always relapse after a time, especially if the acid be not administered continuously, for the achylia is in no way improved. Against the theory it may be argued that marked disturbance of the acid secretion may be found in patients who do not become anemic. But this assertion is usually based on the fact that in many individuals, apparently in perfect health or presenting only gastric derangement, no *free* HCl is found in the stomach-contents. Such disturbances of the secretion, which are by no means always severe, but, in which, indeed, no *free* HCl is found after a test-meal, are often quite wrongly called *achylia*, because sufficient *combined* HCl is present. It should be remembered that the test-breakfast allows of but incomplete conclusions concerning the actual amount of acid secreted during the digestion of an ordinary meal. (See the author's explanations in the discussion of the desmoid reaction, p. 437.) There can be no doubt that a decreased secretion of acid, even to a degree where no free HCl can be demonstrated, may yet suffice to maintain protein digestion and iron absorption. The author has been able to show that not only may no *free* acid be present in cases of pernicious anemia, but that the total acidity is always markedly reduced, and frequently there is no acid at all, the gastric juice being neutral or even alkaline. The severity of the disturbances is shown in these cases by the persistently negative desmoid reaction and the frequent complete absence of pepsin and lab-ferment. That too little attention has

[1] Zeit. f. physiol. Chemie, vol. li, parts 4 and 5.

up to the present been paid to such great and important differences within that large group of gastric disorders characterized by the absence of free HCl (also in stomach pathology) is due, in great part, to the popularity and overestimation of the qualitative tests for free HCl, which, as the author has already pointed out, are inadequate (pp. 437 and 479). The absence of free HCl in the test-breakfast is by no means of the same value in all cases. Besides, it may be that some individuals bear a marked diminution in free HCl better than others. Some have, perhaps, but little need for iron, *i. e.*, there is but slight iron metabolism, so that small traces of iron absorbed from the food suffice to maintain the balance. Variations in the capacity of the intestinal mucosa for absorption also play a part. If once this theory be earnestly tested, it will be demonstrated that the hypochlorhydria of a chronic gastric catarrh can be borne for years, and then finally lead to pernicious anemia through an increase in the disorder or through its long duration. We cannot say how long this latent stage, which ends in outspoken anemia, has lasted; but the fact that years of digestive disturbance often precede anemia leads one to suppose that these cases, too, have passed through a long stage of tolerance. With regard to the final objection that the disorder of the acid secretion may be a *consequence* of anemia, because diminution or absence of free HCl is sometimes, though, by no means constantly, found in other forms of anemia, *e. g.*, chlorosis, it must be pointed out that these secondary disturbances of the acid secretion never attain so high a degree as in pernicious anemia, and that, with the improvement of the anemia, they are improved or cured. This is never the case in pernicious anemia. During periods of improvement the gastric anacidity remains unchanged and is the simplest explanation of the relapse. It is unfortunate that so little work has yet been done to show what happens to the chemistry of the stomach after the parasite has been expelled in bothriocephalus anemia. It is fair to assume that it is improved, because the parasite is of etiologic importance, although the *free* acid, which the author considers irrelevant, may not be reëstablished. The author can report a case, however, where the anemia was cured after the expulsion of the worm, but where, despite the evident dependence of the malady on the parasite, with the return of the gastric disorder later, a fatal recrudescence of the anemia occurred, though at autopsy no evidence of a second bothriocephalus was found. This strongly suggests that bothriocephalus also gives rise to anemia by causing achylia or hypochylia. That the hemolytic properties of the bothriocephalus cannot be taken as the cause of the anemia is shown by the fact that evidences of hemolysis are by no means a part of the symptom-complex of pernicious anemia, especially in the early stage. The significance of the demonstration of hemolytic substances in the bothriocephalus must be considered slight until other intestinal parasites have been studied to determine this property, and until it has been shown that ordinary food-stuffs do not contain hemolytic substances. If, finally, as an argument against the author's theory, we advance the fact that the severest degrees of pernicious anemia may be benefited or temporarily cured by the administration of arsenic, though owing to the continuance of the achylia it may not be assumed that the absorption of iron has been improved, it must not be forgotten that it is quite conceivable that the arsenic stimulates the marrow to increased energy, so that it may get along with even *traces* of iron absorbed from the intestine or may mobilize and make use of the hemosiderin deposits which are always present. The iron theory of pernicious anemia is, therefore, so well grounded, and the arguments opposed to it appear to have so little weight, that it demands serious consideration. The author admits that probably other causes must be considered in certain forms, particularly in the puerperal and in those following syphilis, sepsis, and malaria, especially because the changes in gastric chemistry are not completely understood in those affections, for it is quite conceivable that identical forms of disease of the bone-marrow may arise from different causes.

Differential Diagnosis of Pernicious Anemia.—In contradistinction to most other anemias the diagnosis of pernicious is given in the definition, *i. e.*, in the embryonic type of blood-formation, as shown by the blood-picture. We need, therefore, differentiate it only from those anemias which show a similar type of "hematopoiesis," yet are still separately considered, because pernicious anemia is not yet considered a mere symptom-complex, though this, in the author's opinion, is simply a matter of time. Only the distinctive features of the blood-picture will be discussed here. It is, however, clear that the entire *clinical* picture must be considered in the diagnosis. The differentiation of the so-called cryptogenetic form from those due to helminthes, malaria, sepsis, syphilis, and the puerperal state depends on the demonstration of the cause. The following diseases may be confused with the so-called cryptogenetic or true pernicious anemia:

(1) *Infantile pseudoleukemic anemia* differs from pernicious anemia, first, in the

great numbers of normoblasts which are the rule, while in pernicious anemia they occur in such great numbers only during periods of rapid improvement; second, in the marked leukocytosis; and third, in the much greater increase in the size of the spleen.

(2) *Leukemia* and *pseudoleukemia* may be mistaken for pernicious anemia, especially in the (pseudoleukemic) stages in which the increase in white cells is not striking, for the embryonic type of blood-formation is sometimes observed in these diseases. Most of these cases differ from pernicious by the enlargement of the lymph-nodes, liver, and spleen, besides which the lymphatic forms of these diseases show pathologic lymphoid cells (see p. 793), even if the lymphocytes are not strikingly increased in number.

(3) The *anemia due to malignant tumors* differs in the high leukocytosis, even when the embryonic type of blood-formation is evident. The author has called especial attention to the fact that certain gastric cancers must be recognized as the cause of the genuine prototype of pernicious anemia, which cannot be differentiated from the forms due to achylia (p. 827).

Anemias Following the Loss of Blood

Acute Loss of Blood.—After an acute hemorrhage the blood becomes rapidly diluted, owing to the absorption of lymph and water. Although the hemoglobin and the number of blood-corpuscles may be normal immediately after a hemorrhage, all the characteristics of oligochromemia soon appear, and persist until a normal condition has again been reached. The decrease in hemoglobin may be very marked, to 20 per cent. (corrected) or less. The red cell count may sink to 400,000. At first the color-index is normal, since, of course, the hemoglobin and the red cells are proportionately decreased. The oligochromemia reaches its maximum within a few hours after a slight hemorrhage, but after severe hemorrhages not until about nine days. Evidence of a regeneration of the blood-corpuscles can be found almost as soon as the plasma begins to be replaced. According to the investigations of Ott and Laache, the number of red blood-corpuscles is normal much sooner than the percentage of hemoglobin. This produces a condition similar to chlorosis, the color-index being less than one. Even from the second day on normoblasts, which not infrequently show mitotic figures, are found (p. 786 et seq.). Immature, non-nucleated erythrocytes showing polychromatophilia appear at the same time. In frank hemorrhage basophilic degeneration is rare. It is observed more frequently in concealed hemorrhage when the iron is reabsorbed. At times the blood may fairly teem with normoblasts (blood crises). Poikilocytosis and anisocytosis are also observed. Megaloblasts may likewise be found if the anemia following hemorrhage be of long duration. Confusion with pernicious anemia is, however, unlikely, because of the post-hemorrhagic leukocytosis, usually polynuclear. Even myelocytes and transition forms may be found. The number of blood-platelets is increased and the coagulation hastened after acute losses of blood. Mikulicz considers that major surgical operations will not prove successful if the hemoglobin sink below 30 per cent. This assumption is rather arbitrary, and the percentage of hemoglobin which would justify an operation might very well be placed a little higher, especially if the anesthesia is to be a prolonged one, as anesthesia exercises some detrimental influence upon the composition of the blood.

Chronic Loss of Blood (Hemorrhoids, Menorrhagia, Chronic Gastric Ulcer, Carcinoma, Ankylostomiasis, etc.).—Generally speaking, the condition of the blood here is very similar to that several days after an acute loss. The number of red blood-corpuscles is, as a rule, not diminished to so great an extent as the hemoglobin, probably on account of the processes of regeneration. The color-index is, therefore, less than 1. The anisocytosis and poikilocytosis, though present, also after acute hemorrhage, as well as the megaloblasts, are more pronounced in chronic bleeding. This is, in all probability due to the continued loss of plasma and the permanent hydremic nature of the blood-plasma. Another difference is that the leukocytes are not increased in the severe cases of anemia following chronic hemorrhages, and so the picture approaches more and more that of pernicious anemia, without, however (especially in regard to the color-index and the volume quotient) coinciding with it exactly. The number of polynuclear leukocytes is an approximate measure of the regenerative activity of the bone-marrow in the anemias following hemorrhage. The presence of nucleated blood-corpuscles is another index.

ERYTHREMIA OR POLYCYTHEMIA (POLYCYTHEMIA VERA OR RUBRA, POLYGLOBULIA)

Numerous descriptions have recently appeared, the first coming from French writers,[1] of a peculiar affection of middle-aged adults, which consists essentially of a more or less marked increase of the erythrocytes and of the hemoglobin, associated with splenic enlargement, and, further, is characterized clinically by a marked redness or cyanosis of the face, headache, attacks of vomiting, slight albuminuria with casts, and the presence of blood in the sputum, vomitus, and feces. The autopsy findings indicate that, in addition to the increased number of erythrocytes, there is also a true plethora, since all parts of the body seem to contain an excessive quantity of blood. The heart is normal or somewhat enlarged. In several cases the blood-pressure was found to be increased. The disease appears in middle life and lasts for many years. As yet there is no accurate information as to any change in the bone-marrow. Careful examinations of the blood in these cases show that the number of erythrocytes may be increased to 12,000,000 per c.mm., and the hemoglobin to 200 per cent. (corrected). Such high values are, however, rare. Usually the hemoglobin is about 120 per cent. (corrected) and the color-index is less than 1. The number of leukocytes varies. Türk always found leukocytosis (up to 36,000) in his cases. It may be absent (in about one-half the cases). Myelocytes may be present; the eosinophiles and mast-cells may be increased; polychromatophilia, anisochromemia, normoblasts, and myeloblasts may be noted. The specific gravity of the blood is increased. The same is true of the viscosity of the total blood and of the plasma alone (Kottmann). It is still doubtful whether all cases answering to this description are one and the same affection. Türk believes that, in some of the cases at least, there is a primary hyperplasia of the erythroblastic bone-marrow, with increased function. In favor of this conception is the frequently occurring leukocytosis and the finding of myelocytes. Türk has suggested the name of erythremia or erythrocythemia for this disease, and contrasts it with myeloid leukemia, as the red cell analogue of the latter. The author believes, however, that all cases described in the literature are not to be considered one and the same malady. The blood-picture in chronic stasis may simulate polycythemia because of the retention of the corpuscles in the capillaries on account of the slow current; or polycythemia may result from it, since certain organs, in consequence of this "sifting" of the corpuscles, contain too little hemoglobin, and, therefore, more active blood-formation results, due to functional adaptation of the bone-marrow. The abnormally high blood-counts are in favor of this possibility. It cannot be said that there is no primary erythremia like that described by Türk. However, such a diagnosis should be guarded, and one should not fail to recognize the condition due to stasis. The following case of the author's is interesting from the standpoint of the pathology of erythemia and of iron therapy. A severe chlorosis was so benefited by the administration of iron that the hemoglobin rose to normal and the red cell count to 8,000,000.

[A case of erythremia recently reported by Kinnicut showed the following condition of the blood in addition to the findings noted above: Viscosity 2.7 times normal, specific gravity 1065, total volume of blood per 100 gms. body weight nearly twice normal, red cells 75 per cent. of the volume of the blood. Coagulation time decreased. Stern[2] reports finding a strikingly red marrow in the long bones. It almost, if not quite, replaces the normal yellow marrow. In it there is often a distinct increase in the nucleated erythrocytes. Weber,[3] in an analysis of 25 cases, found that much of the bone-marrow is converted from normal (fatty) to red (active blood-forming). In one case a large proportion of "non-granulated mononuclear myelocytes" or "myeloblasts" were reported. There is thus an increase in erythro- and leukoblastic tissue, the latter often predominating. The splenomegaly seems to be due in part to engorgement, in part, to hyperplasia.—Ed.]

LEUKEMIA

The chief characteristic of leukemia is a considerable and permanent pathologic increase of the mononuclear leukocytes in patients who do not exhibit, aside from

[1] Vaquez, Sem. Med., 1892; Rendu et Widal, Bull. et mém. de la soc. mém. des hôp., vol. iii, Sér. 1899, p. 528. Further references in Türk's article, Wien. klin. Woch., 1904, Nos. 6 and 7; and Stern, Med. Klinik, 1902, Nos. 2 and 3.

[2] Med. Klinik, January 9, 1908.

[3] Weber, Quarterly Jour. Med., October, 1908.

the changes in the blood-forming organs (the bone-marrow, spleen, and lymph-nodes) any other lesions which may be considered primary.

Formerly leukocytosis was separated from leukemia, in a very arbitrary way, according to the degree of increase of the white blood-corpuscles. If the proportion of white to red cells reached from 1 : 50 to 1 : 20, the affection was called leukemia. This method of differentiation was shown to be useless in the early studies of leukemia and in cases of severe leukocytosis associated with marked anemia. When Ehrlich emphasized the frequency of the eosinophilic leukocytes in myeloid leukemic blood, it was at first believed that he had found a reliable point of differentiation between leukemia and leukocytosis, but it did not prove to be a correct one. Since the morphology of the leukocytes has been more accurately studied, it has been found that the difference between leukemia and leukocytosis is neither one of gradation nor one depending upon the tinctorial properties of the leukocytic granules, but that the true difference lies in the fact that in leukemia there is a very great increase in the mononuclear cells which dominate the blood-picture to a marked degree, and may even exceed the numbers of the polynuclear type. However, this does not sharply define leukemia, because there are other diseases with striking increases in the mononuclear elements, and because the blood-picture in leukemia may present wide variations, so that temporarily it hardly differs from that of a leukocytosis or some other blood disease or, indeed, from normal blood. A definite conception of the disease can, in realty, therefore, be formed only from the whole clinical picture and from an understanding of its pathology.

Since *lymphatic* is to be sharply differentiated from *myeloid leukemia*, the pathologic processes which determine the different types must be described separately. But it is necessary to consider the historic development of the classification in order to understand them.

Leukemias were formerly classified, according to the associated changes in the organs, as *splenic*, *myelogenous*, and *lymphatic*, to which transition or mixed forms were added. This classification is no longer tenable from a modern hematologic standpoint. The blood and also the *histologic* changes in the organs, which show, in one case, an increase in the *myeloid*, in another an increase in the *lymphatic*, tissue must nowadays be considered as deciding the classification.

How inaccurate a classification based on macroscopic changes must be, is shown by the fact that such findings cannot be sharply differentiated from one another. Thus, in lymphatic leukemia, for example, even if the hyperplastic lymph-nodes are, as a rule, most striking, yet quite regularly the lymphatic tissue disseminated throughout the body, including that in the bone marrow and spleen, is equally hyperplastic, and the latter organ will be much enlarged. The assumption that a purely splenic leukemia, *i. e.*, one due essentially to disease of the spleen, may occur is equally untenable. Besides, according to recent studies, the spleen has but little to do with blood-formation in adults, and it may be shown that even in those leukemias which seem to deserve the name splenic, because of the great size of the spleen, not only are constant changes found in the bone-marrow, but the spleen itself undergoes *myeloid* degeneration, and it is the *myeloid* elements of the blood which are increased in numbers. Finally, with the establishment of the fact that so-called splenic leukemia is really a myeloid form, the distinction between splenic and myelogenous leukemia loses its old significance. The clinical conception of mixed forms (*e. g.*, the splenolymphatic, lymphatic myelogenous, etc.), is, therefore, of no value, since in this gross sense practically all forms are mixed.

Ehrlich and Lazarus have recommended subdividing leukemia into two types, based upon the blood-examination: lymphoid leukemia or lymphemia and myeloid leukemia or myelemia. The associated changes in the organs may be described in connection with these terms; for instance, a lymphemia with splenic tumor, or a myelemia with a splenic tumor and swelling of the lymph-nodes. Besides the older terms, lymphatic and myelogenous are not analogous to the present ones, lymphoid and myeloid, because with the older names, as the expression myelogenous shows, the old idea of the origin of the increased leukocytes persisted, whereas the terms lymphoid and myeloid refer to the character of the hyperplastic tissue and not to diseased organs. This tissue is known to be disseminated throughout the body or (the myeloid) at least to develop everywhere. The new names lymphoid and myeloid accordingly imply the existence of a systemic disease characterized by hyperplasia of the lymphoid tissue, on the one hand, and of the myeloid tissue, on the other. This involves every part of the body where the anatomic character of the tissue permits. According to Nägeli, the generalization of this hyperplasia does not depend upon metastases, as in the case of malignant tumors, but upon the almost ubiquitous presence of preformed lymphoid tissue, and upon the fact that it, like myeloid tissue,

can be developed everywhere in the adventitia of the vessels, metaplastically. (See Nägeli, Blutkrankheiten and Blutdiagnostik, 1907, pp. 179 and 133.)

Leukemia may, therefore, be defined as a systemic disease, characterized by hyperplasia of preformed lymphoid or myeloid tissue, or of their forerunners, in which, in addition to hyperplasia in the organs, the blood is more or less overrun with hyperplastic cells.

For a long time there has been a tendency to abandon the sharp distinction formerly drawn between so-called lymphoid and myeloid leukemia; because in myeloid leukemia cells resembling lymphocytes do appear in the blood. The phenomenon was originally explained by assuming that the bone-marrow might produce lymphocytes even under normal conditions, so that in a leukemia arising from this organ the lymphocytes would naturally be increased. These were the cases which were formerly termed mixed-cell leukemias, because it was thought that they presented to a certain degree a mixture of the two types of leukemia. One still encounters this expression in the literature.

It is difficult to conceive of the blending of two diseases so fundamentally different, both clinically and morphologically, as lymphoid and myeloid leukemia, because the lymphoid and myeloid tissue and their corresponding cells in the blood, both in their numbers and their proportions, behave like antagonists. Nägeli has, however, the author believes, solved the difficulty by showing that the cells resembling lymphocytes, which are found in large numbers in an otherwise characteristic myeloid leukemia, and which might be called lymphoid cells, are not true lymphocytes, but immature, undifferentiated marrow-cells, which he calls *myeloblasts*. The characteristics which distinguish these cells from lymphocytes have been given above (p. 793, Pl. 5, Fig. 1, *f*, and Fig. 3, No. 21, and Pl. 6, Fig. 2, No. 14).

CHRONIC LYMPHOID LEUKEMIA (CHRONIC LYMPHATIC LEUKEMIA)

(*See Pl.* 8, *Fig.* 4)

The essential characteristic of the blood-picture in this disease is the absolute and relative increase in the lymphocytes up to 90 per cent., or, indeed, to 99 per cent., of the total leukocyte count. The small lymphocytes usually predominate. The absolute number may be several hundred thousand, rarely over one million. There is rarely an absolute increase in the other leukocytes. Myelocytes are seldom present and then sparsely. Eosinophiles and mast-cells are few. The hemoglobin, as well as the number of red cells, may remain normal for a long time. Later there is an oligochromemia and a decrease in the number of the red cells. Then the blood-picture resembles that of pernicious anemia (megaloblasts, normoblasts, anisocytosis, megalocytes, polychromatophilia, and basophilic stippling of the red cells). The blood of chronic lymphoid leukemia has no striking macroscopic characteristics except the oligochromemia; never the yellow color sometimes observed in myeloid leukemia. The dilution made for hemoglobin estimation is often turbid, because the lymphocytes are not dissolved.

Nägeli, in particular, has shown that the lymphocytes present the following variations from normal cells. These are of especial importance in the diagnosis if the increase in the leukocytes be not marked.

1. The protoplasm may be even more scanty than in normal cells, and recognizable only as a narrow margin around the almost naked nucleus.

2. The nucleus often contains less chromatin, and, therefore, when stained, appears lighter than normal. (See Pl. 5, Fig. 3.)

3. The size of the lymphocytes varies more than normally. Besides the small cells, large lymphocytes with pale nuclei are always present. (See p. 793 and Pl. 4, Fig 3.) The number of these cells usually increases during the acute exacerbations of the disease, thus bridging the gap between it and acute lymphoid leukemia. Some of the large lymphocytes show lobulation and cleavage of the nuclei, described by Rieder. (See p. 793 and Pl. 5, Fig. 3, Nos. 22 and 23.)

4. Sometimes these large lymphocytes predominate, as in the case of acute lymphoid leukemia.

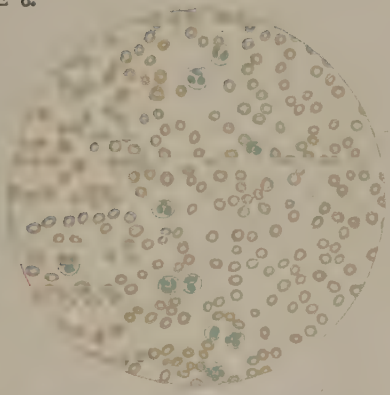
5. The azure granulations present in one-third of all normal lymphocytes are usually absent in lymphatic leukemia (Nägeli). However, the author has also found them in this disease.

The protozoan cellular parasites found by Löwit and Mannaberg, but not confirmed by other writers, cannot be discussed here.

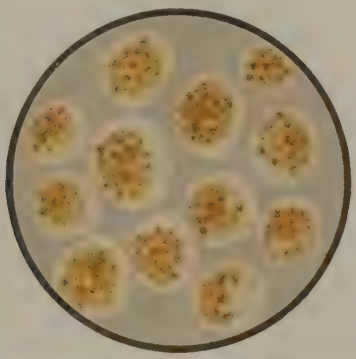
In regard to the other clinical findings, attention should be called to the usually extensive swelling of the lymph-nodes, particularly those of the neck, in which it usually begins. These may vary from the size of a bean to that of an apple. They are usually not adherent to the skin, and rarely break down or discharge, even if they

PLATE 8.

Normal blood. In the field of vision a lymphocyte, a polynuclear cell, and an eosinophile one. The nuclei of all the white cells dark blue, the eosinophile granulations a brilliant red (Rieder).

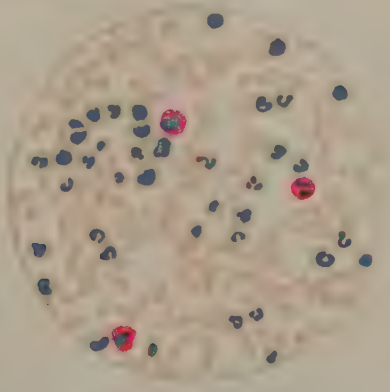


Inflammatory leukocytosis. Marked increase of polynuclear leukocytes. Representation of their neutrophile granules (Rieder).



Heart-disease cells from fresh sputum-preparation (Jakob).

Lymphatic leukemia. Almost all the white blood-corpuscles uninuclear (lymphocytes); most of them very small (Rieder).



Lienomyelogenic leukemia. Most of the white cells are uninuclear; many are strikingly large, with large, plump nucleus. Several eosinophile cells. One nucleus contains red blood-corpuscles (Rieder).

are very soft to the touch. The spleen is almost always enlarged, but usually to a moderate degree, rarely attaining the enormous size of the spleen of myeloid leukemia. The bones may be sensitive to percussion. Affections of the skin are very frequent and quite characteristic of chronic lymphatic leukemia. Pruritus, urticarial eruptions, and lymphoma-like growths of the skin, which may develop into large tumors, occur, particularly in the face (lymphoderm perniciosa). Lymphomatous tumors of the tonsils and of the lingual follicles, as well as of the salivary and lacrimal glands, and infiltration of mucous membranes, may develop, and by ulceration may give rise to hemorrhage. The liver also may be more or less increased in size, sometimes resembling a tumor. The Bence-Jones protein may be demonstrated in the urine. The eye-grounds often show hemorrhages, fatty degeneration, and infiltration of the retina. Even hemorrhages into the skin and mucous membranes may occur.

ACUTE LYMPHOID LEUKEMIA (ACUTE LYMPHATIC LEUKEMIA)

(*See Pl.* 8, *Fig.* 4)

The blood-findings in acute lymphoid leukemia are, on the whole, similar to those of the chronic form, but the oligochromemia is usually much more pronounced. The same turbidity is often noted in the dilutions made for hemoglobin estimations. There are the same predominance of lymphocytes and the same relative suppression of the other white elements. One peculiarity is that the increase in the lymphocytes in some cases (failure of the lymphoid tissue to react) may remain relatively slight (*e. g.*, 20,000). Sometimes, to be sure, excessive numbers (up to 200,000) are present. The counts may be subnormal for short periods at the beginning of the disease and just before death. This last finding shows the transition to acute pseudoleukemia which, under the form of a hemorrhagic diathesis and severe anemia may rapidly prove fatal. The pathologic lymphocytes, especially the larger forms (p. 793), which stain with difficulty, usually predominate. They are of importance in the diagnosis of cases where the number of lymphocytes is not at all or but little increased. However, large forms may be persistently absent from the blood in the acute type. The lymphocytes usually lack azure granulations (Nägeli), in contradistinction to the normal lymphocytes, though the author has found exceptions to this rule, precisely as in chronic lymphoid leukemia.

In its general clinical course acute lymphatic leukemia bears about the same relation to the chronic form as an acute infectious disease of high virulence bears to a milder, chronic infection. It is hardly possible to draw a sharp line between acute and chronic leukemia merely from the duration. The difference between the very acute (lasting a few days) and the very chronic (lasting several years) is quite plain. A sudden onset with pronounced symptoms is particularly characteristic of the acute form. The acute form not infrequently occurs in young people, even in children, whereas to the best of the author's knowledge the chronic form has never been observed in early life. The most acute cases (frequently not diagnosed) may rapidly prove fatal, simulating a severe purpura (so-called morbus maculosus Werlhofii) (p. 841). Other cases assume the characteristics of scorbutus or of a gangrenous (frequently hemorrhagic) septic angina, and are recognized only after examination of the blood. The hemorrhagic diathesis plays an important rôle in the clinical picture of acute lymphoid leukemia. Cutaneous hemorrhages are more common than in the chronic forms, but the skin affections are comparatively rare. The lymph-nodes show less tendency to swelling and may not be enlarged at all—a symptom which is extremely misleading. The spleen is, indeed, enlarged, but less markedly than in the chronic form. The same is true of the liver.

Acute lymphoid leukemia may occur in combination with chloroma (so-called *chloroleukemia*, Nägeli). Its place in the classification is shown in the table on p. 838.

CHRONIC MYELOID LEUKEMIA (MYELEMIA)

(*See Pl.* 8, *Fig.* 5, *Pl.* 4, *Fig.* 2, *and Pl.* 5, *Fig.* 1)

The chief peculiarity of the blood-picture in myeloid leukemia is the presence of numerous leukocytic elements originating in the bone-marrow. The number of such cells is often enormous (up to 300,000 or 400,000 or over). The presence of great numbers of myelocytes is particularly characteristic, although the polynuclear or polymorphonuclear leukocytes usually predominate both absolutely and relatively. The polynuclear neutrophiles may be 80 per cent. of the total count. Even the polymorphonuclear eosinophiles and the mast-cells are absolutely and sometimes relatively increased in number. The neutrophile myelocytes may con-

stitute 40 per cent. of the total count, and the total myelocyte count (neutrophile, eosinophile, and basophile) may exceed that of the polymorphonuclears. The eosinophile myelocytes are numerous, and basophile or mast-cell myelocytes are present in varying numbers. The blood also contains more or fewer myeloblasts, which, according to Nägeli, make up 1 per cent. to 3 per cent. of the total leukocyte count. Large mononuclear cells are scanty, but, according to the author's observations, the transition forms are often numerous. The lymphocytes are relatively diminished, but their absolute number is usually somewhat increased. They are easily confused with myeloblasts, a fact which has led to the erroneous conception of a mixed cell lymphatic myelogenous leukemia in cases where the latter cells are numerous (see below). According to Nägeli, they are best differentiated by the number of nucleoli, lymphocytes never having more than two, while myeloblasts possess three or more (Giemsa's, Leishman, or pyronin methyl-green stains, Pl. 5, Fig. 3, No. 24). The presence of abnormally small, so-called dwarf forms of all varieties of leukocytes, especially the polynuclear neutrophiles and the neutrophile myelocytes, is noteworthy (Pl. 5, Fig. 1). The number and appearance as well as the size of the granules vary greatly. Basophile granulations are found in the eosinophile and neutrophile cells interspersed among the granulations peculiar to the latter. They are regarded as immature forms of such normal granules (Pl. 5, Fig. 3, No. 18). Cells in which the granules are barely visible and appear to be just developing are not uncommon. One should, however, exercise caution in judging of granulations in Jenner, Giemsa, or Leishman preparations. These stains are not always satisfactory and may lead to error, because not all of the granulations are brought out clearly. To the inexperienced observer, the numerous abnormal forms are particularly confusing. They are not always to be classified with absolute certainty, even by an expert. The constant and distinguishing characteristic is, however, the enormous number of mononuclear elements of the bone-marrow, with characteristic granulations, which are, for the most part, neutrophilic, but also in almost every case eosinophilic and basophilic. In making a diagnosis it is strongly advisable not to be content with the relative (percentage) counts of the individual varieties of cells, but to calculate the absolute number. Thus, conclusions as to what cells are really increased in number may be reached, whereas mere differential counts leave one in doubt on this point. Temporary changes in the blood-picture may be represented by curves of the individual cell types.

There is usually moderate oligochromemia and a moderate diminution in the number of red cells. The color-index is about 1. Anisocytosis and moderate poikilocytosis are usually present, while in severe cases megalocytes may be found. As a rule, polychromatophilia, basophilic degeneration, and normoblasts, megaloblasts, and intermediate forms of nucleated red cells are found. The blood-plates are usually increased in numbers.

In consequence of its large content of myeloid cells the blood gives a distinct oxydase reaction (p. 856 et seq.) in the presence of guaiac without turpentine. In severe cases the blood may appear yellowish or ochre colored. The blood and the plasma itself are very viscid (Kottmann), so that good smears are very difficult to make. The dilutions made in estimating the hemoglobin are often turbid from the presence of leukocytes. It is interesting to note that Charcot's crystals have been seen repeatedly in fresh preparations, though, little attention has been paid to them. They seem to depend on the increase of eosinophiles and are regarded as derivatives of the latter. (See p. 707 et seq.)

The blood-picture described above may present many variations even while the patient is under observation. The number of the cells with eosinophile and basophile granulations is particularly variable. According to Lazarus, mast-cells and basophile myelocytes may be 47 per cent. of the total leukocytes. In rare cases the neutrophile cells are very few (Schleip). On account of the unreliability of Jenner's, Leishman's, and Giemsa's stains in this respect the author would strongly advise caution in making such an assumption without studying triacid preparations. Nägeli occasionally found enormous numbers of myeloblasts (in one case, 54 per cent. of 268,000). He calls such cases *myeloblasthemia:* or if such increase be permanent, myeloblastic leukemia. Such cases may be mistaken for lymphoid leukemia. In regard to the avoidance of such mistakes through the distinction of lymphocytes and myeloblasts see pp. 793 and 836. In cases where the myeloblasts are so markedly increased, transition forms between myeloblasts and myelocytes are usually found. These cells resemble myelocytes, but contain few granules. Nägeli, with some reason, considers the alleged transition between myeloid and lymphoid leukemia to be in reality a transition between ordinary myeloid leukemia and myeloblastic leukemia. All kinds of anomalies are observed during the administration of arsenic or treat-

ment with x-rays. It is further noteworthy that in intercurrent infections the total leukocytes may be markedly decreased, so that the blood-picture may be transformed into a simple polynuclear leukocytosis or may become almost normal. Under such circumstances the myelocytes may nearly all disappear. Quincke[1] has observed a similar change after tuberculin injections, and it may occur without evident cause.

Among the other clinical signs of myeloid leukemia should be mentioned, first of all, a frequently enormous increase in the size of the hardened spleen. (See Fig. 170, p. 379.) Over it, one not uncommonly hears perisplenic friction sounds, probably often due to infarction. The liver is usually greatly enlarged. The lymph-nodes may or may not be enlarged. They are seldom so large as in lymphoid leukemia. Chronic nephritis and ascites, the fluid containing myelocytes, are not uncommon. There may be a febrile rise in temperature. The eye-grounds often exhibit hemorrhages, areas of degeneration on the retina, and a peculiar thickening of the vessel-walls, due to infiltration of the adventitia with leukocytes. In the urine, uric acid and alloxuric bodies are often increased, and uric-acid crystals and amorphous urates are found in the sediment.

Löwit's observations of protozoan cellular parasites in the leukocytes have not been confirmed.

The *diagnosis* of myeloid leukemia is usually easy, the more so as the large splenic tumor suggests it and calls for a complete examination of the blood. Despite this, however, there are cases which are difficult to distinguish from marked leukocytosis with numerous myelocytes. According to Engel, these may be 10 per cent. (in diphtheria); according to Nägeli, 25 per cent. (in pernicious anemia complicated by sepsis). In such cases the absence of eosinophiles (except in scarlet fever) and mast-cells usually excludes leukemia. Unless the other clinical symptoms are considered, the large numbers of myelocytes and the high leukocytosis sometimes seen in multiple myeloma (p. 841) and in granuloma (p. 839 et seq.) cannot always be differentiated from myeloid leukemia. The difficulty here probably depends on the fact that in these cases the condition of the bone-marrow is very closely related to, if not identical with, that of leukemia. This applies with equal force to the sometimes striking increase in myelocytes in infantile pseudoleukemic anemia. The facts that the disease runs a more favorable course and that true myeloid leukemia is not apt to occur in early infancy are all that serve to establish a diagnosis. For so-called leukanemia see p. 839.

ACUTE MYELOID LEUKEMIA (ACUTE MYELOBLASTIC LEUKEMIA, NÄGELI)

Acute myeloid leukemia has been recognized but a few years because formerly all acute leukemias were considered lymphatic. The monocellular elements found in the blood of this form resemble lymphocytes. They are, so to speak, lymphoid cells. Careful investigation shows, however, that these cells are the myeloblasts described by Nägeli, *i. e.*, they look like lymphocytes, but belong to the myelocyte order of still undifferentiated marrow-cells. The chief evidence in favor of this view is the presence of transition forms between these structures and the myelocytes. In cases of this disease an enormous number of myeloblasts may be found (up to 75 per cent. of the total leukocytes). The malady may prove fatal in a few weeks, grave symptoms of a hemorrhagic nature, ulcerative stomatitis, and severe anemia supervening. There may be no swelling of the lymph-nodes, and in contrast to the chronic form, even the spleen may be but slightly enlarged.

THE LYMPHOMATOSES AND THE LYMPHOID PSEUDOLEUKEMIAS

Under the name lymphoid or lymphatic pseudoleukemia have been grouped a number of diseases which, although without the typical blood-picture, do resemble leukemia so far as the condition of the lymph-nodes and spleen are concerned and which are, therefore, conceived to be systemic diseases of the lymphoid tissue.

They are probably, however, closely related to leukemia in character, as is indicated by the existence of transition forms of true leukemia. Since the occurrence of transition types between the aleukemic and the leukemic forms, as well as the relationship of the two diseases is generally accepted, lymphoid leukemia and lymphoid pseudoleukemia have been grouped together under the general term lymphomatosis or lymphocytomatosis. In addition the sublymphemic forms are distinguished from the aleukemic and the leukemic, as well as the intermediate types. The interrelations of the individual types are represented in the table below. To

[1] Deut Arch. f. klin. Med., 1902, vol. lxxvi.

complete the presentation of the terminology it may be stated that Pappenheim, regarding multiple myeloma of the bones (Kahler's disease, see p. 841) as the myeloid analogue of lymphoid pseudoleukemia, calls it *myeloid pseudoleukemia*.

Certain types designated *lymphosarcoma* (Kundrat) have been distinguished from the aleukemic lymphomatosis, though they present the same histologic picture. They differ from true sarcoma in this respect, but resemble it in that they are, at least in the beginning, localized and later become general by metastasis after the manner of malignant tumors. The author finds this distinction very difficult to apply. It cannot be considered a criterion for distinguishing infiltrating tumors, and is more properly applied to pseudoleukemic lymphomatosis, as is brought out in the table below, because many cases of the latter which later impress one as systemic diseases may begin as local manifestations. This is true of many lymphomata leading to pronounced leukemia.

Moreover, there has arisen a considerable clinical difficulty since the demonstration of a greater variability than was formerly supposed to exist in the diseases which present the macroscopic picture of lymphoid pseudoleukemia and which are accompanied by generalized enlargement of the lymph-nodes and spleen. Beside, the affections just described, appropriately named pseudoleukemic lymphomatosis, there are others which, despite a superficial resemblance to the general clinical picture of lymphoma, exhibit a very different histology. Instead of an exclusive proliferation of the lymphocytes, we find a polymorphous cell picture consisting of large endothelioid cells, fibroblasts, epithelioid cells, and giant-cells mixed with lymphocytes, thus resembling inflammatory granulation tissue, so that, following the example of Kundrat and Benda, the enlarged nodes have been called granulomata. Even these granulomata are often just as generalized systemic diseases (granulomatosis) as are the true lymphomatoses. Hence the clinical differentiation is naturally very difficult. For some of these (malignant granulomata) no cause has been demonstrated, whereas others, because of their content of tubercles and giant-cells, are known to be tuberculous and still others luetic. These granulomata must, therefore, be distinguished from the true lymphomatoses.

The clinical differentiation of true pseudoleukemic lymphomatosis from granulomatosis is sometimes extremely difficult, because neither influences the blood-picture to any marked degree. The blood in the former, however, usually shows certain distinctive peculiarities which are discussed below.

A Classification of the True Lymphomatoses
(Excluding granulomatoses)

	Generalized.				*Localized but forming metastases.*
	Chronic.		*Acute.*		
	Benign.[1]	*Malignant.*	*Benign.*	*Malignant.*	
1. Alymphemic	True lymphoid pseudoleukemia.	Alymphemic, lymphosarcomatosis.	Acute lymphoid pseudoleukemia.	Alymphemic chloroma.	Lymphosarcoma, strictly speaking (Kundrat).
2. Sublymphemic		Sublymphemic lymphosarcomatosis.		Sublymphemic chloroma.	
3. Lymphemic.	Chronic lymphoid leukemia.	Lymphemic lymphosarcomatosis.	Acute lymphoid leukemia.	Lymphemic chloroma (Nägeli).	

True Lymphoid Pseudoleukemia.—Under this title are usually included the aleukemic and sublymphemic forms of the lymphomatoses, excluding chloromata and the localized lymphosarcomata (Kundrat). The sublymphemic forms are most frequently and most surely to be diagnosed as true lymphomatoses. The characteristic to which Pineus has called attention, and which has recently been considered pathognomonic of these cases, is a so-called relative lymphocytosis. Thus the lymphocytes may make up 70 to 90 per cent. of a normal or slightly increased total count of 5000 to 10,000. This finding indicates the relation of this type to the lymphatic form, *i. e.*, lymphoid leukemia. For, as a matter of fact, the lymphocytes in

[1] The terms benign and malignant are here used in the pathologic-anatomic sense. Malignant refers to aggressive growths which proliferate into and destroy neighboring tissues; benign, to the opposite. The anatomically benign forms may, of course, be malignant from a clinical or prognostic standpoint.

these so-called relative lymphocytoses are also *absolutely* increased, and it would, therefore, seem more suitable to consider not a relative, but an absolute, increase of the lymphocytes as a distinguishing characteristic, and to term it the "sublymphemic constitution," since this would give a clearer idea of the nature of the change. The indefinite boundary between this malady and lymphoid leukemia depends on the nature of the case. A sharp line between pseudoleukemia and leukemia cannot be drawn because, as we have seen, in certain stages of the latter, particularly in *acute* lymphoid leukemia, the lymphocyte increase may be lacking, and, on the other hand, pseudoleukemia may temporarily assume a true leukemic blood-picture. For the diagnosis of this sublymphemic condition it is also essential that there be many lymphocytes of the atypical form described on p. 834 (Nägeli). These cells are not, however, pathognomonic, because they may occur also in other lymphocytoses *e. g.*, in typhoid fever. The blood in these cases shows a certain degree of anemia with the same characteristics as in lymphoid leukemia (p. 834).

The remaining clinical picture of true lymphoid pseudoleukemia is characterized by: (1) Enlargement of the lymph-nodes and spleen; (2) absence of fever and of the diazo-reaction; (3) the frequent appearance of signs of a hemorrhagic diathesis in the later stages; (4) an infiltration with lymphocytes of the skin of the eyelids and mammæ and of the mucous membranes of the mouth, throat, and pharynx.

There are also *acute* forms of lymphoid pseudoleukemia (see table p. 838), which, as morbus maculosus Werlhofii rapidly prove fatal. These are rarely connected with the swelling of the lymph-nodes and need not give rise to any sublymphemic peculiarity of the blood. In such cases the diagnosis is often made only after histologic examination of the lymph-nodes. (See p. 841.)

Kundrat's Lymphosarcoma.—According to Nägeli, the blood-picture of localized, so-called *Kundrat's, lymphosarcoma* differs from that of true pseudoleukemia by the frequent occurrence of a neutrophile leukocytosis and a relative diminution of the lymphocytes. The chief point in the differential diagnosis is, however, the absence of absolute generalization and the relatively slight involvement of the spleen and liver. However, this is not an unrestricted criterion, at least in the early stages, because even true lymphatic leukemia may occur in the form of a tumor limited at first to the cervical or mediastinal nodes. Precisely for this reason, since even the blood-findings are not always decisive, the author considers the clinical diagnosis of Kundrat's lymphosarcoma very difficult.

Granulomatosis.—According to Nägeli, some cases of granulomatosis give rise to a marked neutrophile leukocytosis (up to 50,000), sometimes with eosinophilia and frequently with numbers of myelocytes. The lymphocytes are absolutely and relatively diminished because of the involvement of the lymph-nodes. Sometimes there are periods in which the mast-cells are increased. There may or may not be anemia. Nägeli found polychromatophilia and basophilic degeneration of the red cells without oligochromemia in one case due to tuberculosis.

The clinical picture is, however, to be differentiated from that of true lymphoid pseudoleukemia by the absence of a hemorrhagic diathesis and of infiltration of the skin and mucous membranes. The spleen may be swollen. Fever and the diazo-reaction are frequently observed. There is a characteristic alternation of febrile and afebrile periods (chronic relapsing fever, Ebstein). It is worth noting that in tuberculous granulomatosis the tuberculin test is often negative. The injection of tuberculin into the lymph-nodes should be tried, of course, only with extreme caution. The results of antisyphilitic treatment are naturally of great importance for the diagnosis of specific granuloma.

THE SO-CALLED LEUKANEMIA

Under this name Leube and Arneth,[1] and subsequently Luce,[2] have described blood-affections in which the phenomena of myelogenous leukemia and pernicious anemia occurred simultaneously (myelocytes, megaloblasts, red metaplasia of the bone-marrow). There is no doubt that some of these cases should be regarded as a species of myeloid leukemia. Later observations have shown, however, that these cases hardly form a uniform and independent malady, but that some may be regarded as true pernicious anemia, in which Schindler has proved the presence of myelocytes, and some as myeloid pseudoleukemia. (See Kahler's disease, p. 841.) For a criticism of the theory of "leukanemia" see Morawitz, Deut. Arch. f. klin. Med., 1907, vol. lxxxviii, parts 4 and 5.

[1] Leube, Deut. Klinik, 1902, No. 42; Leube and Arneth, Deut. Arch. f. klin. Med., vol. lxix.

[2] Luce, ibid., vol. lxxvii, parts 3 and 4.

THE BLOOD IN PARASITIC DISEASES

In regard to the eosinophilia occurring in all these diseases see p. 808.

Ankylostoma Duodenale.—The anemia resulting from an infection with this parasite may be of high grade. The red cells may fall to 1,500,000, the hemoglobin to 18 per cent. In contrast to pernicious anemia the color-index is usually less than 1. The author can find no data relative to the presence or absence of megaloblasts. With the increase of the anemia the eosinophiles disappear.

Bothriocephalus Latus.—In those cases which give rise to anemia the picture typical of the pernicious form is presented (with megaloblasts, megalocytes, increase in the color-index, polychromatophilia, and basophile stippling of the red cells, poikilocytosis, and leukopenia). Also aplastic forms without megaloblasts and with a yellow bone-marrow have been described. As the symptoms of anemia become pronounced, the eosinophilia previously present decreases and finally disappears. After the expulsion of the parasite there is usually an immediate improvement or, indeed, a permanent cure. Exceptions to this do, however, occur. The author has personally observed a relapse in a case which showed at autopsy that the parasite had been quite expelled and that the persistent achylia was the deciding etiologic factor. (See p. 827 et seq. on the character and cause of pernicious anemia.)

Tenia.—In the rare cases in which tenia causes a severe anemia the findings correspond to those of pernicious anemia. In such cases also the anemia is not always promptly nor completely cured after the expulsion of the parasite.

Echinococcus.—In this disease there is a practically constant relative eosinophilia, sometimes as high as 57 per cent. of the total leukocyte count. This is a great aid in the diagnosis of doubtful cases. Sometimes there is a slight increase in the total leukocyte count. According to Rossello (Soc. de biol. sem. méd., 1907, No. 47), the eosinophilia persists as long as the parasite lives, but disappears with its spontaneous or operative destruction. If other causes can be excluded, the persistence of eosinophilia after operation indicates the existence of a second echinococcus.

Trichocephalus.—Trichocephalus dispar also may give rise to severe anemia (see p. 524), but not of the pernicious type. More often the leukocytes are increased in number and the color-index is less than 1.

Filaria Sanguinis.—Besides the embryos, eosinophilia, polynuclear leukocytosis, lymphocytosis, and an increase in the large mononuclears may be demonstrated in the blood of patients with this disease.

Distomum hæmatobium (*Bilharzia hæmatobium*) not uncommonly causes severe anemia in addition to the characteristic symptoms referable to the urinary tract. There is a leukocytosis, eosinophiles are present, and the color-index is low.

Trichinosis gives rise to a marked eosinophilia and often to a pronounced leukocytosis (up to 30,000). The former varies directly with the severity of the disease. Sometimes neutrophile as well as eosinophile leukocytosis is found. An increase in lymphocytes and platelets is noted during convalescence (see p. 809, note 1, for references). In regard to the demonstration of trichina embryos in the blood, see p. 823 et seq.

THE BLOOD IN CERTAIN OTHER DISEASES

BANTI'S DISEASE AND SPLENOMEGALY

Banti's disease and splenomegaly must be discussed together because there is no distinct boundary between them, and because in the former the splenic tumor is, at first, frequently the only symptom. The symptom-complex described by Banti includes a marked enlargement of the spleen of great chronicity, usually combined with anemia and sometimes an irregular fever, which, it is claimed, is later combined with cirrhosis of the liver, also of long duration. After a transition period of icterus and digestive derangement, ascites, severe anemia, and sometimes gastric and intestinal hemorrhages supervene and terminate fatally.

We cannot discuss here the quite obscure pathology of this malady. Banti himself assumes that it consists in a primary toxic disease of the spleen which gives rise secondarily to cirrhosis of the liver, with ascites and to severe anemia. Other pathologists consider it merely a form of cirrhosis of the liver. It is still uncertain whether all cases which present Banti's symptom-complex should be classed together. Congenital syphilis, for example, may cause a similar group of symptoms (Chiari). It is naturally difficult to say anything definite about the blood-findings so long as the question whether the disease is a pathologic entity or merely a symptom-complex remains undecided. In one case Nägeli found a diminution of hemoglobin to

70 per cent. and a decrease in the leukocytes to 3000, of which 68 per cent. were neutrophiles, 17 per cent. lymphocytes, and 4½ per cent. eosinophiles. He found a very similar count in an eighteen-year-old girl with syphilitic cirrhosis of the liver. Nägeli also observed polychromatophilia and basophile stippling, and, after a splenectomy, a normoblastic crisis. Senator [1] considers Banti's disease a splenic pseudoleukemia.

Cases of splenomegaly, which do not present all the symptoms of Banti's disease, may probably be regarded as incipient or near forms. Gaucher has described another form of splenomegaly in which sections of the enlarged spleen revealed the presence of large endothelial cells, complexes which were also to be noted in the liver, lymph-nodes, and bone-marrow. It is doubtful, however, if this represent an independent pathologic picture, since similar cells have been found with other splenic tumors, even in Banti's disease. Clinically, cases such as Gaucher's run an extremely chronic course under the guise of an anemia with enlarged liver, but without ascites. Nägeli quotes a case of this kind described by Borissowa in which the blood resembled that of pernicious anemia (high color-index, megaloblasts, and megalocytes), except that there was a leukocytosis. The independence of this disease seems to the author just as questionable as that of the related infantile pseudoleukemic anemia.

[Bovaird [2] reports two cases, one with autopsy, and summarizes as follows: Splenomegaly is a definite and distinct disease; not a new growth, but an endothelial hyperplasia of the spleen associated with like changes in the lymph-nodes and the connective tissue of the liver. Brill, Mandelbaum, and Libman [3] report two cases out of four occurring in one family in a single generation. They confirm Bovaird's findings.—Ed.]

THE BLOOD IN MULTIPLE MYELOMA (KAHLER'S DISEASE)

The malady was recognized as an anatomic entity before Kahler described it clinically. It is characterized by the presence of tumors in the bone-marrow, which arise from the elements of the same (*i. e.*, the myeloid, lymphoid, erythroblastic or other marrow-cells). Metastases may occur outside of the osseous system. The disease affects adults, especially men of advanced age, and is first manifested by characteristic rheumatic pains in the bones, later by progressive cachexia, nervous phenomena, and the presence of the Bence-Jones protein in the urine (p. 570 et seq.), and, finally, by spontaneous fractures, frequently an anemia of high grade, and sometimes fever. The relationship of the disease to leukemia and pseudoleukemia, *i. e.*, to lymphomatoses and blood diseases is not yet fully clear. Some such close relationship does probably exist. Pappenheim regards this malady as the myeloid analogue of lymphoid pseudoleukemia, and terms it *myeloid pseudoleukemia*. Little is known of the blood-picture. Many cases of the so-called leukanemia should perhaps be classed as Kahler's disease. The hemoglobin and the red cell count are frequently both diminished. Though the white cells do not always present abnormal changes, cases with neutrophile leukocytosis and lymphocytosis have been described. Sometimes Türk's irritation forms are found in great numbers (p. 792 et seq.).

THE BLOOD IN PURPURA

It is impossible to draw a characteristic blood-picture for this disease, since even if one exclude cases where the symptom-complex purpura develops from a well-recognized malady (nephritis, leukemia, etc.), the diseases accompanied by purpuric symptoms show no agreement in their etiology. Nägeli, in a study of several cases of so-called simple and rheumatic purpura, was unable to find any striking morphologic changes in the blood. The eosinophiles were only moderately reduced in number.

The blood in the severe form of morbus maculosus (Werlhofii) has no peculiar characteristics. According to the author's experience, these cases cannot be considered one and the same disease. They behave like infections of very different types. It must be strongly emphasized that many cases which were formerly called acute morbus Werlhofii or *purpura fulminans* are really nothing more than the most acute form of *lymphoid leukemia*. (See p. 835.) In these acute cases the swelling of the lymph-nodes is often almost, or quite, unnoticeable, so that mistakes are very easy. The author recently saw a case diagnosed as morbus maculosus Werlhofii which presented all the symptoms of the malady, but in which the diagnosis of acute leukemia

[1] Berlin. klin. Woch., 1901, No. 46, and Deut. Klinik, 1903, vol. iii.
[2] Amer. Jour. Med. Sci., Oct., 1900, p. 377.
[3] Ibid., March, 1905, p. 491, and June, 1909, p. 849.

was established shortly before death by a blood-examination. Nägeli points out that sometimes precisely in these acute cases the lymphocytosis is not very marked, so that the diagnosis must often depend on the demonstration of *qualitative* variations in the lymphocytes, especially the presence of large lymphocytes with pale nuclei, which are usually found in acute lymphoid leukemia (p. 793), and on the demonstration of the forms with lobulated or cleft nuclei described by Rieder (p. 793). Furthermore, Nägeli calls attention to the fact that there are also cases of acute aleukemic lymphomatoses (acute lymphoid pseudoleukemia) which may resemble morbus maculosus Werlhofii throughout. Here also the demonstration of the abnormal lymphocytes mentioned above is of great importance in the diagnosis.

THE BLOOD IN SCORBUTUS AND IN BARLOW'S DISEASE

In but few cases of scorbutus has the blood been studied, and nothing characteristic has been found. Oligochromemia dependent chiefly on the degree of hemorrhage has been demonstrated. The red cells are usually less markedly decreased than the hemoglobin. In accord with other inflammatory symptoms the leukocytes are quite markedly increased (up to 60,000, Senator). Besides this, myelocytes normoblasts, and megaloblasts are found. In any case the examination of the blood is of great aid in avoiding confusion with hemorrhagic lymphomatoses or leukemia and pseudoleukemia. Infantile scurvy (Barlow's disease) offers no more characteristic a blood-picture than scorbutus in adults. Senator (Berlin. klin. Woch., 1902, No. 20), De Bruin (Nederl. Tijdschr. von Genesk., 1902), and Wynhausen (Arch. f. klin. Med., 1908, vol. xcii), have found oligochromemia, polychromatophilia, poikilocytosis, normoblasts, and especially a relative and absolute lymphocytosis. The last, however, is present even in normal children.

THE BLOOD IN HEMOPHILIA

But few complete examinations of the blood in this disease are extant. In agreement with Wright the author found in three cases a relative lymphocytosis without any increase in the total count. This naturally means a corresponding decrease in the polynuclears. This finding, however, does not seem to be constant, since Morawitz and Lossen[1] found in one case approximately normal numbers of polynuclears and lymphocytes. Once the author found an increase in the eosinophiles, and at another time a moderate number of myelocytes. Morawitz and Lossen also found that the blood-platelets are essentially normal. On account of this practically characterless blood-picture all the more stress must be laid on the defective coagulability of the blood.[2] (See p. 742.)

THE BLOOD IN MYXEDEMA

J. Bence and K. Engel[3] found in myxedema a relative lymphocytosis and an eosinophilia with a decrease in the absolute number of polynuclears.

THE BLOOD IN EXOPHTHALMIC GOITER

The blood-findings in this disease have only recently been described. Caro[4] found that a marked diminution in the polynuclear leukocytes and a corresponding increase in the lymphocytes up to 50 per cent. is characteristic. The small lymphocytes predominate.

THE BLOOD IN MALIGNANT TUMORS

As is well known, malignant tumors often give rise to anemia, chiefly through the general cachexia, and the hemorrhages, sometimes, also, through the progressive destruction of the bone-marrow by metastases. This anemia is usually accompanied by leukocytosis, and, as a rule, the hemoglobin index is less than 1. Polychromatophilia and basophile degeneration of the red cells are very frequent. Nucleated red corpuscles, if present, are usually normoblasts. They may be numerous if there be metastases in the bone-marrow. Megaloblasts and megalocytes are rare. The

[1] Morawitz and Lossen, Deut. Arch. f. klin. Med., 1908, vol. xciv, parts 1 and 2.

[2] See p. 741 et seq. and Sahli, Zeit. f. klin. Med., 1903, vol. lvi, also Morawitz and Lossen, *loc. cit.*

[3] Bence and Engel, Wien. klin. Woch., 1908, No. 25.

[4] Berlin. klin. Woch., 1908, No. 39.

anemia may, especially in gastric cancer, reach a high grade, and may exceptionally assume all the characteristics of the pernicious type; thus the color-index may be greater than 1, the leukocytosis be replaced by leukopenia, and the normoblasts by megaloblasts. All this arises not from the occurrence of metastases in the bone-marrow, but from the gastric achylia, as in true pernicious anemia (p. 826 et seq.). Such cases have been spoken of as cancer complicated by pernicious anemia; it would seem to the author more accurate to speak of gastric carcinoma as the occasional, though rare, *cause* of pernicious anemia. In such cases the diagnosis between pure pernicious anemia and an anemia of pernicious type following cancer can, of course, not be made from the blood. Should there be no tumor the decisive symptoms are the bacteriologic findings in the stomach-contents (p. 477), the demonstration of stasis and of lactic acid and other signs of gastric carcinoma. Very frequently the occurrence of leukocytosis is a symptom of great weight in the differential diagnosis.

Following metastases of malignant tumors into the bone-marrow numerous large mononuclear cells have been found,[1] which Nägeli calls myeloblasts. Myelocytes also may occur, sometimes in great numbers. With extensive metastases into the lymph-nodes there may at first be a lymphocytosis; this, however, becomes less and less as the lymph-nodes are progressively destroyed, and is finally replaced by a lymphopenia. In the early stages of malignant tumors the eosinophiles may be increased; but in the cachectic stage they are, on the contrary, usually less than normal.

THE BLOOD IN PAROXYSMAL HEMOGLOBINURIA

During the paroxysms of hemoglobinuria poikilocytosis and fragmented blood-cells are found, as well as the so-called erythrocytic shadows (ghosts, see p. 785). No morphologic changes have as yet been noted during the intervals. In contrast to the old theory of periodic hemoglobinuria and to the findings in toxic or infectious hemoglobinuria, the blood-serum of the patient is free from hemoglobin during the attacks. (Demonstration of hemoglobin in the serum, p. 855.) This is explained by Choroschilow's[2] supposition that paroxysmal hemoglobinuria depends on a lessened resistance of the red cells to the action of cold, as, for instance, the application of cold to the body surface; but that the injured cells first yield their hemoglobin while in the kidneys, and that immediately upon its liberation it is excreted. To explain this Choroschilow further assumes that the injured cells act as a specific stimulant to the kidney, to withdraw from them their hemoglobin-content and excrete it. The harmful action of cold may best be demonstrated by drawing the blood from the finger-prick into a capillary tube, provided with an ampulla, which is immersed in iced water and allowing it to lie thus for twenty minutes. The use of the capillary tube is essential for obtaining a thin layer of blood corresponding to that in the skin capillaries. The serum expressed from the clot is colored red in contrast to the normal serum (dissolved hemoglobin). If, however, the coagulation of the chilled blood be hindered by the addition of 0.1 per cent. sodium oxalate solution, no red color is imparted to the plasma. In other words, the expression of hemoglobin in this experiment is dependent upon coagulation; whereas in vivo, it depends upon the action of the kidney. One can establish the diagnosis of this disease by performing the above experiment. During the attacks the blood clots unusually fast, but after a little time the clot is redissolved (Hayem and Chvostek).

THE BLOOD IN CHRONIC LEAD-POISONING (SATURNISM)

The diagnosis of chronic lead-poisoning which, in doubtful, especially in medico-legal, cases formerly sometimes offered great difficulties is much easier with the aid of a blood-examination. This intoxication often gives rise to anemia, *i. e.*, to oligochromemia, which may, however, be lacking despite the pallor of the patient. If it be present, normoblasts, anisocytosis, poikilocytosis, polychromatophilia, and, according to Grawitz, even megaloblasts may be found. There are no data concerning the color-index. [Ewing, Buchanan, Cabot, Emerson, and Nägeli all report a color-index less than 1.—Ed.] Basophilic degeneration of the erythrocytes is especially characteristic and of great importance in the diagnosis (p. 784)—all the more so if there be no very marked oligochromemia, for in other severe anemias it is usually found. Little weight should be put on isolated examples of basophile stippling, since they may be noted even in normal individuals (P. Schmidt, Rosen, and Biber, p. 784). The leukocytes are usually normal. It is not known whether or not leuko-

[1] See Schleip, Zeit. f. klin. Med., 1906, vol. lix.
[2] Zeit. f. klin. Med., 1907, vol. lxiv, parts 5 and 6.

penia be present in severe anemias due to lead-poisoning. Grawitz claims that myelocytes are sometimes found. Besides aiding in the diagnosis of fully developed cases, the demonstration of basophilic stippling is of use in predicting the development of the same, and, therefore, is of value in prophylaxis. In regard to the prognostic value of variations in the number of stippled red cells see p. 784.

THE BLOOD IN PHOSPHORUS-POISONING

Pisarski [1] found that in mild as well as in severe cases of phosphorus-poisoning after a longer or shorter time a transitory polycythemia supervenes (polycythemia vera seu rubra, p. 832), and that in severe cases there is a leukopenia affecting the polynuclear leukocytes only, which, in favorable cases, is replaced by a leukocytosis. In mild cases the leukocyte count is normal. After the poison has been eliminated, normoblasts appear.

THE BLOOD IN ICTERUS

Besides bile-pigment in the blood-serum (p. 857), crenation and lack of rouleaux formation may be noted in fresh preparations of the blood of jaundiced patients (Gerhardt). In icterus neonatorum O. Silbermann found megalocytes, microcytes, poikilocytes, and erythrocytic shadows (p. 785). Despite the destructive influence of the bile salts Becquerel and Rodier found an increase in the number of red cells. Observations concerning the hemoglobin content are not uniform. In severe icterus the percentage is difficult to determine because of the presence of bile-pigment. In regard to the resistance of the red cells to hemolysis in different icteric conditions and the diagnostic significance of this phenomenon see p. 768 et seq.

Georgi[2] claims to have found the characteristic blood-picture of pernicious anemia in a case of jaundice following cholelithiasis. This claim was, however, made at a time when the definition of pernicious anemia was not so strict as at present. This question is of considerable practical importance because there are not a few cases of pernicious anemia which are complicated by hematogenous icterus and intermittent fever. If Georgi's contention be correct, one would have to make, in such cases, a differential diagnosis between cholelithiasis and pernicious anemia. It is, however, according to the previously quoted studies, quite unlikely that a chronic obstructive jaundice can give rise to a blood-picture characteristic of pernicious anemia, because, outside of the fact that no authentic observations of such a sequence have been recorded, the red cells in the former condition show an increased, in the latter a decreased, resistance to hemolysis (p. 770). The practical significance of this is shown in the following case—that of a patient with pernicious anemia and jaundice whose gall-bladder was opened because the surgeon wrongly diagnosed a cholelithiasis on account of the icterus and the periodic rises in temperature so common in pernicious anemia, and this contrary to the advice of the attending physicians, who supported their view by careful blood-examinations, and in spite of the fact that nothing pointed to a cholelithiasis and that the temperature was not accompanied by local symptoms, but merely by an increase in the jaundice and in the excretion of urobilin.

The leukocytes vary greatly according to the cause of the jaundice. Limbeck found a leukopenia (4000 to 7000); Grawitz, sometimes a marked leukocytosis (30,000 to 40,000). Data concerning the reasons for these variations, as well as differential counts, are as yet unavailable.

THE BLOOD IN BRONCHIAL ASTHMA

While the presence of eosinophile cells in the sputum has been recognized for a long time, there are but few studies extant concerning the behavior of the blood in this disease. In general an increase in the eosinophiles has been claimed (p. 808). According to an observation made by Heineke and Deutschmann,[3] there was a moderate neutrophile leukocytosis at the beginning of the attack. The number of eosinophiles rapidly dropped below normal, then rose above normal, and ultimately normal figures were reëstablished. In addition, lymphocytosis was noted in connection with the attack. These observers, therefore, assume that the eosinophile cells in the sputum arise from the blood, and are not, as has been claimed, histogenetic. The nuclei of the eosinophiles in the blood were frequently but indistinctly lobulated, or were merely indented, so that it may be assumed that the mononuclear cells in

[1] Deut. Arch. f. klin. Med., 1908, vol. xciii, part 3, p. 308.
[2] Quoted from Grawitz, Klinische Pathologie des Blutes, Berlin, 1896, p. 197.
[3] Münch. med. Woch., 1906, No. 17.

the sputum, the occurrence of which suggested the histogenetic theory, arise from eosinophiles in the blood which undergo secondary changes within the bronchi. (In regard to eosinophile cells in the sputum see Fuchs, Deut. Arch. f. klin. Med., vol. lxiii.)

THE BLOOD IN BURNS

In three fatal cases of burns of the first to the third degrees Hedinger found peculiar malformations of the red cells, spheric forms, thick disk forms, crenation and bell shapes; also mutilated structures resembling the blood-platelets. These formations correspond to the artefacts produced by heating blood to 50° to 60° C. They agree with the older findings of Albrecht. Hedinger explains the changes by assuming a melting of the lipoids in the superficial layers of the red cells. The "platelets," which are probably not true blood-plates, may contain hemoglobin, but may also appear quite colorless.

OSMOTIC PRESSURE OR MOLECULAR CONCENTRATION OF THE BLOOD

In contrast to cryoscopy of the urine, which received a rather adverse criticism upon p. 666 et seq., we possess in cryoscopy of the blood an extremely valuable method of examination. It furnishes important conclusions, particularly in the diagnosis of functional diseases of the kidneys. It cannot be replaced by the determination of the specific gravity of the blood-serum, since to get results analogous to those obtained from the osmotic pressure the albumin must be removed from the blood-serum, and the complete removal of so large a quantity of albumin is possible only after a preceding dilution. Moreover, in view of the small quantities of blood usually at our disposal, the specific gravity must be determined by the rather troublesome capillary-pyknometric method of Hammerschlag. (See p. 735.)

The nature of the osmotic pressure and its measurement by determinations of the freezing-point, or cryoscopic examination, have been explained on p. 662 et seq. In reference to the technic the reader is also referred to what has previously been stated in detail (p. 663 et seq.). Only those features which are peculiar to the cryoscopy of the blood will now be discussed.

The determination of the freezing-point of the blood is usually carried out by withdrawing rather a large quantity of blood (usually about 20 cc.) from the patient by venesection (see p. 731) and allowing it to coagulate. The separation of the serum from the clot may be accelerated by loosening the latter from the sides of the vessel. This serum is then employed for the examination. The freezing-point, or osmotic pressure, of the serum is practically equal to that of the plasma, because fibrin, in consequence of its great molecular weight and of the small percentage present, exerts practically no influence upon the lowering of the freezing-point. Since the osmotic pressure of the serum is equal to that of the plasma, it must also be equal to that of the whole blood or of the defibrinated blood, since the blood-corpuscles must necessarily possess the same osmotic pressure as that of the plasma. It consequently follows that the osmotic pressures of the serum, of the plasma, of the whole blood, and of the defibrinated blood are identical. Nevertheless, we do not recommend the employment of the whole blood unless hirudin has been added, because it can be used only after coagulation, and with this semi-solid mass, even though it be stirred, we have no guarantee that the temperature is absolutely homogeneous. It is only when a sufficient quantity of serum cannot be obtained that the coagulated whole blood may be employed, and then it should be well broken up by the platinum stirrer after its introduction into the freezing apparatus and before the determination is made. It is better previously to defibrinate the blood. This may readily be accomplished immediately after its withdrawal by stirring it in a glass vessel for some time with the platinum stirrer belonging to the freezing apparatus. In every case all the hemoglobin should be changed into oxyhemoglobin before coagulation and separation of the serum, since the blood obtained by venesection always contains a large quantity of CO_2, and since the variable quantities of CO_2 found combined or free in the blood are dependent upon the degree of oxidation of the hemoglobin, so that this naturally has some influence upon the osmotic pressure. Besides this, anions go over from the plasma into the corpuscles where the blood is rich in CO_2. (See p. 851.) Constant results will be obtained only when the blood employed is saturated with oxygen. This saturation with oxygen is most easily insured by allowing the blood from the cannula to trickle in a thin layer along the sides of the receiving vessel. The contact of the blood with atmospheric air is sufficient to convert all its hemoglobin into oxyhemoglobin; the area of contact may be increased by catching the blood in a funnel

introduced into the mouth of the receiving vessel, and then markedly tilting the funnel so that the blood will spread out in a thin layer upon its inner surface and trickle slowly into the receptacle. Where the blood has been defibrinated, the stirring necessary for that purpose is sufficient to convert the reduced hemoglobin into oxyhemoglobin. Some investigators also pass oxygen into the blood, but this seems superfluous to the author and too complicated for clinical purposes. It might also be noted that it does not matter whether or not some of the erythrocytes remain in the serum (as frequently happens), since defibrinated blood and serum have the same freezing-point.

The normal freezing-point of the blood is $-0.56°$ C., corresponding to that of 0.9 per cent. NaCl solution.

The most important result of the determination of the freezing-point of the blood is that it gives definite information in reference to the sufficiency or insufficiency of the elimination of urinary solids by the kidneys. When the method is accurately carried out with due regard to the previously mentioned precautions, among which the author would lay special stress upon the saturation of the blood with oxygen, a depression of the freezing-point amounting to 0.01° to 0.02° must be regarded as pathologic. Considerable elevations of the osmotic pressure of the blood are most frequently encountered in uremic conditions when freezing-points of —0.65° and —0.7° C. are by no means rare. This evident disturbance of the elimination of urinary solids undoubtedly has some relation to uremia; but the idea that an elevation of the osmotic pressure is constantly present in uremia is incorrect, as is also the converse—that uremic symptoms must be present when the osmotic pressure is increased. From this it follows that uremia is not dependent upon the elevation of the osmotic pressure alone, but must be due to the retention of some special substances.[1] This retention cannot be recognized from the freezing-point of the blood when the retained substance is compensated for, from an osmotic standpoint, by the elimination of other solids. Disregarding the question of uremia, the determination of the freezing-point of the blood furnishes the most important data for the estimation of the work done by the kidneys in a given case of nephritis, and consequently justifies important conclusions in reference to treatment. The author would call special attention to the fact that, while all conclusions in reference to the renal function based upon cryoscopic examination of the urine are inaccurate except in extreme cases, a renal insufficiency may be surely concluded from a distinct elevation of the osmotic pressure of the blood, and this must be considered in deciding for or against unilateral nephrectomy, though, to be sure, more recent experiments have shown that a moderate depression of the freezing-point of the blood does not always contraindicate this operation.

Very considerable elevations of the osmotic pressure of the blood have also been observed in cardiac cases with broken compensation.[2] Since uremic symptoms, in the ordinary sense of the word, are scarcely ever present in these cases, it follows that uremia does not essentially depend upon the elevation of the osmotic pressure of the blood.

The osmotic pressure of the blood may be lowered in the retention of water as the result of nephritis, in case this retention is not compensated for from an osmotic standpoint by the simultaneous retention of urinary solids, as is usually the case. If the loss of osmotic pressure be more than compensated, cryoscopy is of no value for the recognition of hydremic plethora, and we must then employ what is really the best method for this purpose, the determination of the relative quantity of hemoglobin in the blood. (See p. 731.)

The lowering of the osmotic pressure of the blood indicative of the retention of water in febrile diseases is also of general pathologic interest.[3]

INVESTIGATION OF THE VISCOSITY OR OF THE INTERNAL FRICTION OF THE BLOOD

The clinical importance of the determination of the viscosity of the blood rests upon the fact that, according to the laws of Poiseulle and Hagen concerning the flow of liquids through capillary tubes, this quality is an essential factor in determining the velocity of the blood-current. From the physicochemical investigations of

[1] From the constant findings of Strauss in his analyses of the blood in uremia these retained substances are nitrogenous, and consist largely of urea.

[2] Landau, Arch. f. klin. Med., 1904, vol. lxxviii.

[3] See Landau, ibid.

Ostwald[1] and the physiologic study of the question by Hürthle,[2] C. Hirsch and C. Beck[3] have worked out a clinical method for determining at the bedside the viscosity or internal friction of the blood. The apparatus employed is illustrated in Fig. 314. The method depends upon measuring the time required by a known quantity of blood to flow through a capillary tube under a definite pressure. The experiment must be carried out at a constant temperature, since the temperature influences the viscosity. The apparatus[4] is constructed as follows: It consists of the hand-bulb *A*, of the calcium chlorid tube *B*, of the pressure flask *C*, which is protected against heat-conduction and radiation by a felt jacket; of the manometer *D*, which is rendered more sensitive by being filled with benzol; of the water-bath *E*, and of the actual measuring apparatus *F*. This measuring apparatus consists of a U-shaped tube, *XV*, which is dilated at *G*, below which it becomes capillary, to dilate again at the bend *U*, and pass into the ampulla *M*, in which the closed tube *V* is inserted by means of a ground joint. There is a mark both above and below

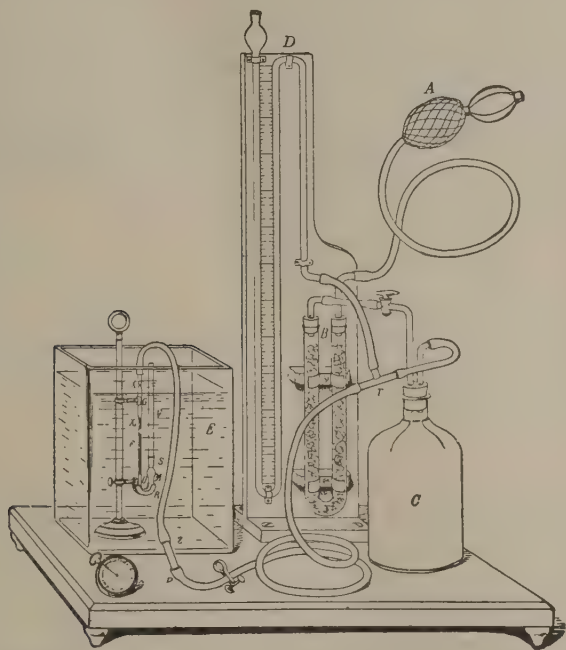


Fig. 314.—Apparatus of C. Hirsch and C. Beck for the determination of the viscosity of the blood.

the dilatation at *G*. The capacity of *G* is about ½ cc., and the diameters of the different capillary tubes vary between 0.25 and 0.35 mm. During the course of the experiment this measuring apparatus is held by a support, as indicated in the figure, immersed in a water-bath at a temperature of 38° C., and connected by the T-tube *T* and tubing with the pressure flask *C*, the calcium chlorid tube *B*, the hand-bulb *A*, and the manometer *D*, as indicated in the illustration. The upper end of the closed tube of the measuring apparatus projects into the air above the level of the water. Before commencing the experiment, the measuring apparatus should be kept for some time in air at a temperature of 38° C., so that we may be certain that its temperature is 38° C. immediately after its immersion in the water. Beside the appa-

[1] Physicochemical measurements.
[2] Pflüger's Arch., vol. lxxxii, parts 9 and 10.
[3] Münch. med. Woch., 1900, No. 49, and Arch. f. klin. Med., vol. lxix.
[4] Made by C. Desaga, Heidelberg.

ratus is a stop-watch which registers fifths of a second. The experiment now proceeds as follows: The connection is broken at *P;* the tube leading to the pressure flask is closed by a stop-cock, and the desired pressure of 400 mm. of water, equal to 452 mm. of benzol, is obtained in the pressure flask by means of the hand-bulb. The U-shaped lower portion of the measuring apparatus is now filled to the upper end of the ampulla (*M*) with blood, which is obtained fresh from an exposed vein in the arm by means of a pointed and bent glass cannula or the sharp metal cannula mentioned on p. 731. If the latter be used, it is not necessary to expose the vein, though this procedure has the advantage that the blood can be obtained without the production of artificial stasis. The closed tube *V* is now quickly inserted. Suction is then made at *Z* until the blood is just above the mark *X*. The measuring apparatus is now connected with the pressure flask by the glass tube *Z P*. The stop-cock is opened so that the pressure forces the blood downward through the capillary tube. The stop-watch is set going as soon as the upper level of the blood-column passes the upper mark *X*, and is stopped at the moment when it reaches the lower mark X_1. The experimenter notes the elapsed time, convinces himself that the pressure has remained constant, and immediately repeats the measurement. In this manner from two to six measurements may be made with the same blood. The manipulation must be done very quickly, so that it may not be interfered with by coagulation. According to Jakoby,[1] blood may be employed which has been rendered non-coagulable by the addition of leech extract or hirudin. This does not influence the result, while defibrinated blood exhibits a diminished viscosity. This procedure has been used in the author's clinic with success. The addition of hirudin facilitates the estimation of the viscosity, for one is not compelled to hurry. One mg. of hirudin is sufficient to prevent the coagulation of 5 cc. of blood. The apparatus is cleansed with soda solution and distilled water and kept in a dry place.

The necessary calculation is made by the formula—

$$n = n_1 \frac{st}{s_1 t_1},$$

in which n is the desired coefficient of the internal friction of the blood, s the specific gravity of the blood, n_1 the coefficient of the internal friction of the fluid with which the blood is compared, s_1 the specific gravity of this fluid, and t and t_1 the flowing-times of the two fluids. Freshly distilled anilin is selected for comparison, since its specific gravity is so close to that of the blood that it may be assumed to be equal to it. This simplifies the formula, so that—

$$n = n_1 \frac{t}{t_1}.$$

It also appears to the author that in the Hirsch-Beck method, where, in contrast to Ostwald's, gravity is not a factor, the specific gravity must be left out of the equation.

n_1, the coefficient of viscosity of anilin, is compared with that of water (which serves as the unit in these investigations), is determined once for all, and it consequently follows that, in order to calculate n, we must simply determine the flowing-time of anilin $= t_1$. We then know the value of n_1 and t_1, and, as we have determined t for the blood, the formula gives us the value n; that is, the coefficient of the viscosity of the blood as compared with water. Since interest centers chiefly in relative values, it is still simpler for clinical purposes to select the viscosity of anilin as the unit This gives us—

$$n = \frac{t}{t_1}.$$

In order to obtain the coefficient of water from this, one must multiply n by the coefficient of anilin compared to water. According to Hirsch and Beck, this is about 3.75. Since the foregoing study, still other methods for determining the viscosity of the blood have been devised. The following are the best known.

The viscosimeter of Robert-Tissot[2] is based on another principle. The viscosity

[1] Sitzung der medic. Gesell. in Göttingen, January 10, 1901. Ref. in Deut. med. Woch., 1901, No. 8.

[2] Folia Hematologica, 1907, vol. iv, part 4.

of the blood is estimated by determining the decrease in the amplitude of oscillation of a gold-plated metallic cylinder suspended in blood, which has been rendered non-coagulable by means of hirudin. The cylinder of a Pravaz syringe with which the blood has been withdrawn serves as the containing vessel after the plunger has been removed, the point of the syringe being closed with a rubber cap. The cylinder is warmed to 38° C. before the blood is withdrawn, and during the experiment is kept in a chamber heated to this temperature.

The Viscosimeter of W. Hess.[1]—Hess uses, as do Ostwald, Hirsch, Beck, Determann, and others, the rate of flow of blood through a capillary tube, but with the difference that he does not determine the relation of the flow for a given amount of blood to the same amount of water, but the relation of the amounts of water and of blood flowing for a given interval of time. No hirudin is used.

The description of the apparatus and the method is given in the author's words.

"On an opalescent glass plate *H* are fastened two graduated tubes (Fig. 315), *A* and *B*, both of which communicate, on the one hand, with the tube *G*, and, on the other, with the bulb *L*, by means of the rubber tube *K*.[2]

"The two tubes are narrowed at the other end into capillaries, *C* and *D*, having a very fine bore. Further on they widen out into tubes *E* and *F* of the same caliber as that of *A* and *B*. The tube *F*, which fits on *H*, is held in place by the spring *N*. This tube can be removed, and can be replaced by other tubes of similar dimensions. By means of the stop-cock *Q* one is able to bring *B* into communication with *G* and to cut off the communication with the bulb *L*. The tubes *A* and *B* are bent at right angles before they communicate with *G*, so that they, with the tube *K*, enter the tube *G* from above. Between the tube *K* and the bulb *L* is interposed a piece of glass tubing *V*, in which is a small hole which permits communication of the system of tubes with

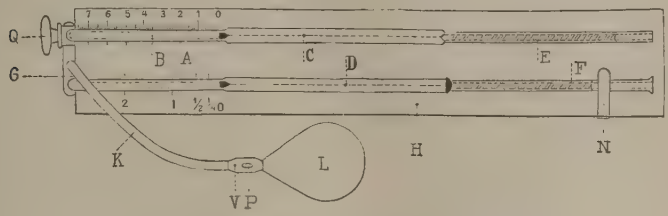


Fig. 315.—Viscosimeter of Hess (seen from above).

the air. The plate *H* is fastened in a case which contains all the other parts of the apparatus, tubes to replace *F*, a bottle of ammonia, a thermometer, etc. The dimensions of the case are 27 × 9 × 6 cm.

"The determination is carried out in the following way: In the tubes *B*, *C*, and *E* is placed a column of water so that the left end of the column is exactly at the zero mark of the scale. The stop-cock is closed and so shuts off communication of the system *B C E* with the bulb *L*. Before the tube *F* is placed in position, it is filled with a drop of blood which is run in by capillary attraction. After placing in position, the blood is sucked into the capillary tube and into the tube *A* by means of the bulb, *L*. When the blood has reached the zero point in the tube *A*, as is shown in the figure, the stop-cock *Q* is turned, and the bulb is, therefore, in communication with the system *B C E*. By further suction *B* is filled with water from *E* through the tube *C*, while at the same time blood flows into *A* under the same pressure. As soon as the latter has reached the mark 1, the pressure is removed by releasing the finger from the opening *P*, so that both water and blood remain stationary. The amount of water which has flowed into the tube *B* can be read off on the scale and this shows the relative viscosity of the blood to the water. By pressing the bulb *L* both water and blood are driven back. When the former has reached the zero point, one closes the stop-cock *Q* and empties the blood completely from *A* and *D*. The tube *F* is

[1] Münch. med. Woch., 1907, No. 45.

[2] The bulb *L* is used for pressure and for suction. Pressure is obtained by closing the hole *P* with the finger and pressing the bulb. Suction is obtained by pressing the bulb and then closing the hole *P*. When the pressure is released from the bulb suction is produced. By removing the finger from the hole both pressure and suction are stopped.

removed and is replaced for the next experiment by a fresh one. By washing out *D* and *A* twice with ammonia the apparatus is ready for another experiment."

The principal objection which can be raised to the apparatus of Hess is that the action of the ammonia remaining in the apparatus may change the viscosity of the blood. This is not the case, for the blood which comes in contact with the ammonia solution is not used for the determination of the viscosity. That part of the blood which is contaminated with ammonia at the time the blood is placed at zero has left the capillary and is to be found in the shaded part of the tube *A*, where, owing to the relatively wide caliber of the latter, it does not influence the viscosity. In other words, in setting the scale, the ammonia is removed from that part of the apparatus which is used for the determination of the viscosity, so that the blood used for this purpose may be regarded as free from ammonia.

The tubes *F* are washed out, and allowed to stand in ammonia. When a number of them are used up, they are dried by heating them on a metal plate. One may avoid cleaning them by purchasing a large number and throwing them away after once using. Their cost is nominal.

If a sample of blood be very viscous, it is sucked up only to the mark ½ or ¼, and the results multiplied by 2 or by 4.

Control tests with the apparatus with fluids of known viscosity give an error within 1 to 2 per cent.

Hess found that on raising the temperature 1 per cent. the viscosity decreased 0.8 per cent., so that tests which are performed at room temperature may have an error of about 4 per cent. According to Hess, such an error may be neglected when the variations which are found in pathologic conditions are taken into consideration. He considers that a temperature correction is only necessary where the temperature difference is considerable.

The mathematic and physical principles for the method are given in Hess' paper (Vierteljahrschr. der Züricher Naturforsch. Gesellschaft, Jahrg. 51, 1906[1]).

Hess found that the value at 37° C. was about 17 per cent. lower than at 17° C. If one wish to reduce the value to the temperature 17° C., one must subtract 0.8 per cent. for every degree above this temperature The estimations which are made at room temperature, however, give sufficiently accurate values for clinical purposes, and may be used without recalculation.

On the other hand, Hess has found that the withdrawal of the blood must be done with certain precautions, for if this be not done, the values with the same individual may vary as much as 8 per cent. This is not due to any inherent defect in the method, but to the fact of varying conditions of circulation at the point of withdrawal. Hess found, as have others, that local venous stasis may increase the viscosity. Massage of the skin decreases the viscosity. In order to make the conditions as comparable as possible, Hess recommends that the patient place the finger in warm water and massage it well in drying it. The values so obtained are nearly those of arterial blood.

Concerning the clinical value of viscosity determinations one must concede that the practical results are so far not altogether certain. The older investigations are contradictory, due to the fact that most of the determinations were performed with blood which was removed from a vein in the arm during marked venous stasis. According to the degree of stasis, the results are invalidated to an extent which cannot be estimated. Although stasis raises the viscosity, the values found may lead to errors in both directions because stasis may act more in one case than in another, and one may observe a decrease in the relative viscosity of one case to another when there is actually an increase. Since no estimations of the viscosity of blood taken from a vein in the arm, with the exception of those where the vein has been exposed (p. 848), are free from the above objections, both the methods of Hess and of Determann, which use a small quantity of blood, taken either from the ear or from the finger-tip, represent a distinct step forward.

A necessary condition for the clinical use of the determination of the viscosity of the blood is some knowledge of the normal relations of the viscosity and of the changes under physiologic conditions. F. Blunschy,[2] under the direction of Hess, has recently given some information on this subject.

The principal results of the investigation with Hess' method are as follows: The diurnal curve for the viscosity of the blood shows a curve which falls from 8 A.M., rising toward 9 P.M. The minimum is found between 2 and 6 P.M. The

[1] The apparatus is to be obtained from J. G. Cramer, Glasbläserei, Spiegelgasse 7, Zürich, 1. The price is 32 Marks.

[2] I. A. D., Zürich, 1908, Beiträge zur Lehre von der Viscosität des Blutes.

morning maximum at 8 A. M. varies between 5.68 and 4.41; the minimum in the afternoon can sink as low as 3. It is remarkable that the increased viscosity is due to assuming the erect position, because, after rising, the viscosity goes up sharply, and then commences to fall, while persons who remain in bed do not have the fall during the morning. The intake of food and fluids decreases the viscosity, as does moderate bodily exercise. Violent exercise increases the viscosity (due to perspiration). Alcohol and caffein increase the viscosity; coffee decreases it, as does camphor. Digitalis administered to healthy subjects is without effect. In general disturbances of the circulation and the respiration Blunschy found, as have other observers, that viscosity is increased. Inhalation of oxygen decreases the viscosity. This agrees with Hamburger's observations[1] that increased content of the blood in carbon dioxid produces profound chemical changes, as the osmotic pressure of the corpuscles increases, due to the passage of anions into them from the plasma. They, therefore, increase in size. This naturally produces an increase in the viscosity of the whole blood.

Somewhat far-reaching conclusions have been drawn from the fact that the viscosity of the blood increases with increased content in carbon dioxid, and with better aëration the viscosity decreases. There can be no doubt that the general condition of a patient suffering from the increased viscosity of the blood acts as a hindrance to the circulation. If one wish to use these facts clinically, one must not forget that one cannot use the determination of the viscosity of the blood to diagnose a functional disturbance of circulation, for primary disturbances of the respiration act on the viscosity of the blood in precisely a similar way. One must also remember that local changes in the circulation may, through their influence on the distribution of the blood-corpuscles, affect the viscosity. (See p. 850.) Hess has shown how one may avoid the last error. (See p. 850.) Of the other important results which have been furnished by Hess, one may add that the assumption that the heart changes which are observed in nephritis are due to an increased viscosity of the blood has been confirmed neither by Hess, Hirsch and Beck, nor by other authors. Kottmann (*loc. cit.*) found that the viscosity of the plasma was increased in nephritis, but this cannot be considered as a hindrance to circulation as long as the total viscosity of the blood is not increased. Potassium iodid decreases the viscosity.[2] The viscosity is decreased in anemia.[3] Cold baths and electric sweat baths increase, warm baths decrease, the viscosity (Determann, *loc. cit.*). Polycythemias increase the viscosity markedly (Kottmann, *loc. cit.*). Leukemia with marked increase in leukocytes increases the viscosity if the number of erythrocytes be not decreased sufficiently to compensate.

The viscosity after meat feeding is greater than with a vegetable diet (Determann, *loc. cit.*). After the intravenous injection of saline solution and after the withdrawal of blood the viscosity decreases. It has been generally assumed, and the assumption has been confirmed directly by Blunschy, that the viscosity of the blood is principally due to the number and size of the formed elements, especially of the erythrocytes.[4] The investigation of the plasma gives much smaller variations.

As average values for the viscosity of the blood compared with water, Hirsch and Beck (without hirudin, blood at 38° C., water at 38° C.) give 5.1. Kottmann (hirudin, venous blood, blood at 38° C., water at 38° C.) gives 5.1. Determann (hirudin capillary blood, blood at 38° C., water at 38° C.) gives for men 4.798; for women, 4.516. As normal average values for his method and for room temperature, 20° C., Hess[5] gives the value 4.57; for men, 4.3 to 5.3, and for women, 3.9 to 4.9. Hess has obtained a quotient by dividing the relative hemoglobin value by the viscosity. The result is a number which varies between 17 and 21, but which is mostly in the neighborhood of 19. In pathologic conditions he finds variations from this number.

The present condition of the subject of the viscosity of the blood has been brought together by J. Heusler in a recent dissertation (Zürich, 1908). The literature on the subject is given there.

[1] Osmotischer Druck und Ionenlehre, 1902.

[2] Poiseulle, Ann. de chimie et de physique, 1847. According to this author sodium iodid does not act in this way. See Müller and Inada, Deut. med. Woch., 1904; Kottmann, Korrespondenzbl. f. Schweiz. Aerzte, 1907, Nos. 4 and 5.

[3] Determann, Zeit. f. klin. Med., 1906; Kottmann, *loc. cit.*

[4] Besides the excess of carbon dioxid, this is perhaps another and more important reason why one finds too high values for the viscosity of the blood when the blood is taken from an occluded vein.

[5] Hess, Arch. f. klin. Med., vol. cxiv, Nos. 3 and 4, p. 404.

CHEMICAL EXAMINATION OF THE BLOOD

(Percentage of hemoglobin, see p. 742. Reaction of the blood, see p. 736. Removal of the blood for the purpose of chemical examination, see p. 731.)

IRON TESTS FOR THE BLOOD WITH JOLLES' FERROMETER

A. Jolles [1] has devised a method for determining the amount of iron in the blood by means of an instrument called a ferrometer.[2] The method requires only small amounts (0.05 cc.) of blood. Its principle is, briefly, as follows: A measured quantity of blood (0.05 cc.) is removed with a special capillary pipet (such as is used in Gowers' hemoglobin examination, p. 744). It is reduced to an ash in a platinum dish, 0.1 of acid potassium sulphate is added, and the mixture is heated and evaporated to dryness. The residue contains the iron of the blood in the form of an oxid of iron. This is dissolved in 10 cc. of hot water and 1 cc. of diluted hydrochloric acid (1 in 3), and 4 cc. of ammonium thiocyanate solution (7.5 : 1000) added, so that the total quantity is 15 cc. This gives the red solution of ferric thiocyanate, whose composition can be determined colorimetrically by comparing it with a solution containing a known quantity of iron. The latter is prepared in such a way that each cubic centimeter contains exactly 0.00005 of iron.[3] One cc. of this standard solution is diluted to 10 cc. with water, and then 1 cc. of dilute hydrochloric acid and 4 cc. of ammonium thiocyanate solution are added just as above. The resulting solution is then, by means of the apparatus pictured in Fig. 316, compared colorimetrically with the ferric thiocyanate solution derived from the blood. This apparatus consists of two glass cylinders, *C* and *C′*, of exactly equal caliber, *C* containing accurately 15 cc., and *C′* about 16 cc. Both cylinders are subdivided into 0.1 cc., and both are closed at the bottom with glass plates, through which light is reflected from the plaster-of-Paris reflector *R*, in the direction of their axes. The ferric thiocyanate solution prepared from the blood is exactly 15 cc., and so just fills the cylinder *C*, which is then covered with a glass disk, care being taken to avoid the formation of air-bubbles. Fifteen cubic centimeters of the ferric thiocyanate solution (prepared from the stock solution) are placed in cylinder *C′* for comparison. To avoid the development of a meniscus, which will disturb the reading, a floating stopper, made of aluminum and closed at both ends with parallel glass plates, is placed on the surface of the fluid in cylinder *C′*, avoiding air-bubbles. A flat fluid surface is thus obtained. This contrivance always displaces a slight amount of fluid, which is the reason why cylinder *C′* must be made somewhat taller than *C*. Cylinder *C′* is provided with a lateral escape stop-cock, *H*. Both cylinders can be easily removed from the base of the instrument for cleansing or filling. The tin jacket surrounding the cylinders shuts out any lateral illumination. The colorimetric comparison is made as follows: Both cylinders are filled as just described, and then the fluid in *C′* is allowed to escape through the stop-cock *H* into the vessel *A* until the contents of both tubes, as seen from above by transmitted light, present exactly the same shade. When this point is reached, cylinder *C′* is removed and the level of the fluid noted. If the amount of fluid remaining in *C′* to the base of the floating cork were exactly 15 cc., the amount of blood used (0.05 cc.) would contain 0.00005

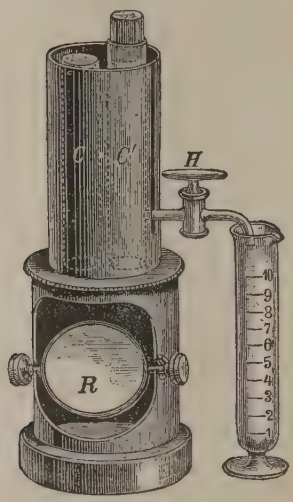


Fig. 316.—Jolles' ferrometer.

[1] Deut. med. Woch., 1897, No. 10; ibid., 1898, No. 7, and Pflüger's Arch., vol. lxv.
[2] Made by C. Reichert, Wien, Bennogasse.
[3] For the exact steps see above reference. The fluid may be obtained from the manufacturer of the instrument.

of iron, *i. e.*, 1 liter of blood would contain 1 gm. of iron. If, however, when the color in the two cylinders is alike, C' contain only 7.5 cc. of fluid, the amount of iron contained is only half as much, *i. e.*, 0.5 gm. per liter of blood. A table to calculate the percentage of iron contained in the blood has been prepared by Jolles, and is included with the instrument. It takes about ten to fifteen minutes to estimate the amount of iron with Jolles' ferrometer.

The same maker (Reichert) has recently placed upon the market an instrument which may be used either as a Fleischl-Miescher hemometer or as a Jolles' ferrometer, since the intensity of the color of the ferric thiocyanate solution is estimated by means of the glass wedge of the hemometer.[1]

Jolles believed at first that his method was an accurate means of determining the amount of hemoglobin indirectly, for he assumed that hemoglobin contained 0.42 per cent. of iron, and that all the iron present was contained in the hemoglobin. But in more recent communications [2] he has abandoned the theory, as his investigations have led him to conclude that the blood contains considerable quantities of iron, probably in the shape of nuclein, outside of the hemoglobin. This idea corresponds to the views of Biernatzki and Jellinek. Moreover, it is likely that hemoglobin itself does not always contain a constant amount of iron. The great variations (which have been reported) as the result of analyses of hemoglobin crystals in one and the same animal species would seem to suggest this.

Although these statements might seem to imply that the estimation of the iron in the blood might acquire a clinical significance independent of that of the estimation of the hemoglobin, the investigations of Krüss [3] and Schwenkenbecher [4] would make this seem very doubtful, since these writers reached the conclusion that the double ferric thiocyanate producing the red color in Jolles' method becomes so markedly dissociated by dilution that the red color decreases in intensity more rapidly than does the quantity of iron in the solution. In other words, iron cannot be accurately estimated by this colorimetric method.[5]

ESTIMATION OF THE AMOUNT OF ALBUMIN IN THE BLOOD, ACCORDING TO DEYCKE AND IBRAHIM

The method, the details of which will be found in the original paper (Zeit. f. klin. Med., 1906, vol. lviii, Nos. 5 and 6) is a modification of the titration method of Denigés for the determination of albumin in the urine.

THE ESTIMATION OF THE AMOUNT OF GLUCOSE IN THE BLOOD

The detection of glucose in the blood is simple, if one remove the albumin by the method given under the uric-acid estimation (p. 855). In the filtrate the presence of sugar can be demonstrated by the ordinary reactions (p. 586). The filtrate can also be used to determine the amount of sugar quantitatively. For this purpose the author's modification of Pavy's method is useful. (See p. 620.) According to Claude Bernard, the removal of the albumin may be effected by adding to the blood an equal weight of sodium sulphate, boiling and filtering the mixture. Pavy removes the albumin by allowing the blood to run into 20 times its volume of absolute alcohol, filtering, and evaporating the filtrate as nearly as possible to dryness. The residue is dissolved in a volume of water equal to that of the blood used. The amount of glucose may then be determined by any of the methods, including that of Pavy, and the accurate fermentation saccharimeter (p. 624 et seq.).

The staining reaction which diabetic blood gives with methylene-blue may be mentioned here. Brehmer [6] stains dried preparations of blood which have been prepared by the method given on page 773, and which have been fixed by heating for ten minutes at 135° C. with a 1 per cent. aqueous solution of methylene-blue. Diabetic blood remains almost unstained by the treatment or takes on a bluish-

[1] S. Jolles, Berlin. klin. Woch., 1899, No. 44, p. 965. [2] *Loc. cit.*

[3] Colorimetrie und quantitative Spectralanalyse in ihrer Anwendung auf die Chemie, Hamburg and Leipzig, 1891, p. 176.

[4] Arch. f. klin. Med., vol. lxxv, parts 3–5.

[5] [The objections to the procedure of Jolles have been overcome by Marriott and Wolf, Jour. Biol. Chem., i, 451, 1906. This method consists in performing the reaction in acetone in the presence of ammonium thiocyanate in large excess. The determination of iron in blood and tissues by the colorimetric method is then of great accuracy.—C. G. L. W.]

[6] Centralbl. f. inn. Med., 1897, No. 22.

green tinge, while normal blood is stained intensely blue. Many other stains show a similar difference between diabetic and normal blood. The Brehmer reaction is also to be found in leukemia, nephritis, and multiple neuritis. If, by means of a proper diet, the urine become free from sugar, the staining reaction is not observed. Williamson[1] gives another reaction with methylene-blue, which obviously has nothing in common with the Brehmer reaction. It depends on the reducing action of glucose on methylene-blue. To 40 c.mm. of water, measured with the hemometer capillary pipet (see p. 744), 20 c.mm. of blood from the finger, 1 cc. of a 1:6000 methylene-blue solution and 40 c.mm. of sodium hydroxid solution of the pharmacopœia are added. The mixture is heated in boiling water for three to four minutes without shaking. If the blood be that of a diabetic, the mixture loses its color, while with normal blood the blue color persists.

THE BLOOD IN CARBON MONOXID POISONING

In marked cases of carbon monoxid poisoning the naked eye can probably appreciate the change of color in the blood. It is noticeably bright red, and almost fails to exhibit the difference between venous and arterial blood. The presence of carbon monoxid in the blood is demonstrated usually by means of the spectroscope. (See p. 544 et seq.) If a few drops of blood containing carbon monoxid be diluted with water, the mixture will show in the spectroscope two bands, between the green and yellow, very much like those of oxyhemoglobin (Fig. 233, 1). They are, however, very slightly nearer the violet end of the spectrum. They differ from the oxyhemoglobin bands by not disappearing upon the addition of ammonium sulphid, whereas the oxyhemoglobin bands are replaced by a simple band of reduced hemoglobin (Fig. 233, 2). Oxyhemoglobin bands disappear very slowly after adding ammonium sulphid to the blood, and may be temporarily reproduced if the liquid be shaken with air, owing to the concentrated action of the oxygen.

Another test for carbon monoxid in the blood consists in adding a little 10 per cent. caustic soda or potash solution to the blood contained in a porcelain dish, and then gently warming. If carbon monoxid be present in any appreciable quantity, the mixture will become very brilliant red, while normal blood will turn to a dirty greenish brown.

v. Horszkiewicz and Marx (Berlin. klin. Woch., 1906, No. 35) have very recently proposed the following test, which so far has not been used clinically. The blood is mixed with an 8 per cent. solution of quinin hydrochlorid in the proportion of 2 : 4 (2 cc. of blood to 4 cc. of quinin solution). The mixture is heated with a gas-flame until it boils. After cooling so that the mixture can be shaken without discomfort, 2 or 3 drops of fresh ammonium sulphid solution are added and the mixture shaken well. Blood containing carbon monoxid gives a bright carmin-red color, while normal blood treated in this way is a dirty brownish green.

It is advisable to perform both spectroscopic and chemical tests and compare them with the normal blood for a control, because when only a slight amount of carbon monoxid is present in the blood, quantitative differences are important in forming an opinion.

We must not overrate the diagnostic value of these investigations. The human body reacts so intensely to carbon monoxid gas that symptoms of poisoning may be very pronounced without its being possible to demonstrate the presence of this poison in the blood either chemically or spectroscopically. The author has observed such cases. In any case an examination which is not carried out immediately after the intoxication may fail, if the poisoning has not been too severe, for in these cases the carbon monoxid is rapidly carried away by the lungs.

[1] Lancet, 1900, August 4.

THE BLOOD IN METHEMOGLOBINEMIA

The blood contains methemoglobin in various intoxications, especially those due to chlorate of potash and antifebrin. Its presence is demonstrated by means of the spectroscope after sufficiently diluting the blood with water. (See Fig. 233, 3.)

THE BLOOD IN HYDROGEN SULPHID POISONING

In severe cases the color may be a dirty green, and may show the characteristic bands of sulphohemoglobin, besides the oxyhemoglobin bands. The former resemble the bands of methemoglobin, but are situated a little more toward the violet end of the spectrum (Fig. 233, 3).

THE BLOOD IN HYDROCYANIC ACID AND POTASSIUM CYANID POISONING

A small amount of the blood is dissolved in water, and dilute potassium ferricyanid added. Normal blood becomes brown, owing to the formation of methemoglobin. Blood containing hydrocyanic acid remains red. (Formation of cyanmethemoglobin.) A control reaction should be carried out with normal blood.

DEMONSTRATION OF HEMOGLOBIN IN THE BLOOD-SERUM

Hemoglobinuria may appear independently as the so-called periodic hemoglobinuria (Lichtheim), or especially in certain kinds of poisoning (potassium chlorate, toluylendiamin, nitrobenzol, truffles) and after burns. It is always produced by the solution of red blood-corpuscles within the vascular system. Hemoglobinuria is, therefore, usually associated with hemoglobinemia or methemoglobinemia. An exception is found in the periodic or paroxysmal cold hemoglobinuria in which the serum does not contain hemoglobin. The reason for this exception is discussed on page 843. Free hemoglobin and methemoglobin can be readily demonstrated in the blood by allowing several cubic centimeters of blood to coagulate. Under normal conditions the serum will only be stained slightly yellow (lutein), provided that the blood-clot has not been interfered with mechanically. In hemoglobinemia, on the other hand, the serum will be more or less of a ruby red, owing to the presence of hemoglobin in solution; or brown, if methemoglobin be present. The serum, however, must be absolutely clear, for if it be cloudy, the color may be due to an admixture of blood-corpuscles with the serum, from some disturbance during coagulation. In doubtful cases the microscope will decide the question. The stained serum will give the characteristic bands of oxy- or methemoglobin, one or both, in the spectr scope (Fig. 233, 1 and 3). The characteristics of the blood in periodic or paroxysmal hemoglobinuria are given on page 843.

PRESENCE OF URIC ACID IN THE BLOOD

Physiologically, the blood does not contain any appreciable quantity of uric acid. In chronic nephritis and acute articular rheumatism mere traces only have been found; but in gout, at least in the early stage of the attack, the amount of uric acid contained in the blood is so considerable that Garrod [1] devised a comparatively simple method, the so-called thread test, to demonstrate its presence.

According to Garrod, 30 to 35 cc. of blood are allowed to coagulate; 10 cc. of the serum which accumulates during the next few hours over the clot is mixed with 100 cc. of acetic acid.[2] A fine linen thread [3] is placed in the mixture, which is then covered so as to prevent evaporation, and allowed to stand.

If the blood contain at least 0.0025 per cent. of uric acid, characteristic crystals (Fig. 253) will appear on the thread in the course of one or two days. In doubtful cases the murexid test (p. 673) may be applied to these crystals.

Garrod indirectly demonstrated an increase of uric acid in the blood in gout by performing this test with the serum of an artificially produced blister.

Garrod has been able to demonstrate the increased uric-acid content of the blood in a more satisfactory manner. The blood is allowed to clot, and 60 cc. of the serum is dried on the water-bath. The dried residue is pulverized, and extracted with boiling alcohol, and the extracted powder is then treated with boiling distilled

[1] A. B. Garrod, Gout and Rheumatic Gout, London, 1876.

[2] Thirty per cent. solution according to Minkowski.

[3] It is better not to use a thread, but to separate from it one of the elementary fibers of which it is composed.

water. A few drops of the watery solution are evaporated with nitric acid to dryness, and the residue exposed to the fumes of ammonia. The characteristic purple color of the murexid test is produced (p. 673). Another portion of the aqueous solution is evaporated to a thin syrup, and a few drops of hydrochloric acid added. The characteristic uric-acid crystals will be produced. Another portion is allowed to stand without the addition of acid. At the bottom and on the walls of the vessel will be deposited crystals of sodium urate. Garrod found that in non-gouty subjects the crystals of uric acid were but rarely produced by this method. Garrod made quantitative estimations and found the amount of uric acid in the blood to vary between 0.003 and 0.0175 per cent.

Von Jaksch [1] gives the following procedure for the determination of the amount of uric acid in the blood: 100 to 300 cc. of blood are diluted with three or four times its volume of water. The mixture is heated on the water-bath, and when coagulation commences, a few drops of acetic acid (S. G. 1.0335) are added until the mixture is faintly acid. The fluid is allowed to remain at boiling temperature for fifteen minutes, filtered, and the residue washed with hot water. If the filtrate be not perfectly clear, a small amount of sodium chlorid may be added, and the filtrate heated again with acetic acid on the water-bath and refiltered. After cooling sodium phosphate is added to prevent the precipitation of uric acid, and the amount of uric acid in the mixture estimated by the Salkowski-Ludwig method. The filtrate obtained by this method is, after the addition of HCl, evaporated to 10 cc., and allowed to stand for twenty-four hours (p. 638). Crystals of uric acid are precipitated and collected on a weighed asbestos filter, washed with water and with alcohol, and weighed. They should show the characteristic form on microscopic examination. They may also be tested qualitatively by the murexid test. In case no crystalline precipitate is obtained, the solution may be evaporated to dryness and tested by the murexid test.

Von Jaksch was able to detect uric acid in the blood after it had been freed from albumin by Hopkins' method. (See p. 639.) The method may be carried out by adding to the filtrate from the coagulated albumin 20 grams of ammonium chlorid, and allowing the mixture to stand in a cool place for twenty-four hours. The uric acid is precipitated as sodium urate and may be identified by the murexid test.

Kowarski's method for uric-acid determinations may be similarly employed. (See p. 639.)

Von Jaksch found that the blood under normal conditions did not contain notable quantities of uric acid, but large quantities—up to 0.008 gm. in 100 cc. of blood—were found in pneumonia, affections of the kidneys, in diseases associated with dyspnea, especially heart affections and pleurisy. This is not the case in acute rheumatic arthritis and typhoid. In spite of the fact that an increased amount of uric acid is not pathognomonic for gout, it appears to the author that the differentiation of gouty affections of the joints from those of rheumatic origin by means of the determination of uric acid in the blood is of considerable diagnostic importance, especially if the quantitative estimation give results within the values given on p. 856. In fact the demonstration of increased amounts of uric acid in the blood is frequently the only means of differentiating gouty joint affections from those which are not.

THE OXIDASE REACTION OF THE BLOOD

The neutrophile leukocytes, but not the lymphocytes, contain an oxidizing ferment which changes the color of guaiacum resin solutions without the addition of hydrogen dioxid or oil of turpentine.[2] This property of the leukocytes can be shown in the blood itself, most easily in myelogenous leukemia. According to Nägeli, the reaction is carried out by dissolving a few drops of blood in 2 to 4 cc. of distilled water, thus setting free the oxidizing ferment. The blood solution is then overlaid with a solution of gum guaiacum in alcohol (p. 574, note 1). After a time the ring of contact becomes green to blue. The color is not, however, permanent. If the test be negative, the blood solution, before the addition of the guaiacum solution, may be allowed to stand

[1] Zeit. f. Heilk., 1890, xi, 415; Fodor, Centralbl. f. klin. Med., 1895, xvi, 865.
[2] E. Meyer, Münch. med. Woch., 1903, No. 35.

for twenty-four hours in order to set free more of the ferment and then overlaid with the resin solution. The reaction cannot be confused with the ordinary hemoglobin reaction, for with this test either oil of turpentine or hydrogen dioxid is necessary. According to Nägeli, this reaction is positive in cases besides those of myelogenous leukemia when the leukocyte count is above 20,000. According to this investigator, only the older neutrophile cells give the reaction, for he found in an acute case of myeloid leukemia that the reaction was negative, owing to the predominance of myeloblasts.

In making the test it is necessary to make a control to be certain that the guaiacum solution does not become blue from contact with water alone. This takes place with certain samples of the gum, and also when ordinary tap-water containing traces of iron is used instead of distilled water. Instead of the gum one may use a colorless alkaline solution of phenolphthalin (not phenolphthalein). This changes in the presence of an oxidizing ferment into phenolphthalein, which gives a red color with alkalis.

TESTS FOR BILIARY PIGMENTS IN THE BLOOD

The investigation of the blood-serum for biliary pigments has often afforded the author valuable information where it was necessary to determine the presence of an affection of the liver in the absence of jaundice, or where the discoloration of the patient's skin was doubtful. This method seems to be particularly important in the diagnosis of difficult cases of cholelithiasis or cirrhosis of the liver. In these cases bile-pigments may be found in the blood where the urine yields a negative test. In order to test for bile-pigment one or more cubic centimeters of blood are withdrawn from a vein with a Pravaz syringe, the blood is allowed to coagulate in a test-tube, and to stand until a sufficient amount of serum is expressed from the clot. Serum containing bile-pigments is usually to be distinguished by its marked yellowish or greenish color. The foam produced on shaking is distinctly yellow. If sterile serum be allowed to stand at body temperature for some hours, it gradually assumes a greenish color (von Jaksch). Gmelin's reaction (see p. 575) gives a positive test. The coagulum produced by the nitric acid is greenish in color. Warming the serum for fifteen minutes to 60° C. may also produce a green color. Normal serum does not give this reaction. More information is needed to decide whether, under certain conditions, the lipochrome and lutein of the blood may not give similar reactions. Regarding the morphologic characters of blood in jaundice and the resistance of the red cells see pp. 844 and 770.

EXAMINATION OF THE BLOOD-SERUM FOR UROBILIN[1]

A definite volume of serum is shaken with chloroform. An emulsion is formed which may be separated either by centrifuging or in the following way. Into the neck of a funnel is introduced a piece of absorbent cotton large enough to absorb the larger part of the emulsion. The emulsion is poured on the cotton, which is pressed down with a glass rod. The liquid will then flow into a test-tube placed underneath the funnel in two separate layers. The chloroform solution is then removed with a pipet, and an alcoholic solution of zinc acetate (0.1 per cent.) is added until no more turbidity takes place. If urobilin be present, a distinct green fluorescence will appear.

DIAGNOSIS BY AGGLUTINATION TESTS. GRUBER-WIDAL SERUM-TEST IN TYPHOID FEVER, AND OTHER ATTEMPTS TO MAKE USE OF AGGLUTINATION IN DIAGNOSIS

The Gruber-Widal test is based upon the fact that the blood-serum of patients who are convalescing from typhoid, or of animals immunized to typhoid, according to the investigations of Gruber, Durham, and Pfeiffer, influences the typhoid bacilli

[1] According to Guiart and Grimbert, Précis de diagnostique chimique, etc., Paris, Rudeval, 1906.

in a test-tube in such a way that the latter lose their motility and form clumps which may be recognized microscopically. A similar phenomenon is observed when cholera-immune sera are added to cultures of cholera bacilli. This phenomenon has been attributed to the presence of peculiar hypothetic substances in the immunized serum, which have been called agglutinin or glabrificin by Gruber, and paralysin by Pfeiffer.[1] These substances are not identical with the bactericidal nor immunizing substances of immune serum.

Based upon this observation, Widal[2] devised a peculiar diagnostic method for recognizing typhoid, for he noticed that this peculiarity is shown not only by the serum of convalescents, but also by the serum taken during the disease, and even quite early in the attack. He proposed two methods for testing the serum-reaction of the questionable typhoid cases—the so-called microscopic and macroscopic methods. To prevent evaporation, a few drops of freshly drawn blood are put into a closed tube of narrow caliber. The small vials in which homeopaths dispense their sugar pills may be used, or the blood may be drawn into Wright tubes, which are afterward sealed in a flame and in which it may be preserved for several days. After coagulation the serum expressed from the clot or that obtained by centrifuging is pipeted off. The serum which separates by spontaneous coagulation is employed. In the beginning Widal demonstrated the reaction microscopically by simply adding a drop of the serum to a drop of typhoid broth culture, of not more than twelve to twenty-four hours' growth, upon a slide. Under the microscope the bacilli in the broth culture must show very active movement. If the reaction be positive, the bacilli will cease to move within from a few minutes to half an hour and become clumped, while the intervening fluid will be free from bacilli. The second method depends upon the macroscopic appearance of a typhoid broth culture to which the serum of the patient in question has been added. The control culture is evenly clouded, but a culture to which a moderate amount of typhoid serum has been added will clear up, on account of the agglutinated bacilli settling to the bottom of the tube.

It has, however, been demonstrated in the Bern Clinic that this macroscopic serum reaction is not nearly so reliable as the microscopic test.

To obtain reliable results, the microscopic reaction had to be modified, since it was found necessary to take into account the dilution of the serum, for it was soon discovered that in low dilutions the serum of some people not suffering from typhoid had a moderate power of agglutinating typhoid cultures. It was therefore found necessary to determine that a certain very small quantity of the serum

[1] Van Calcar (Dialyse, Eiweisschemie und Immunität, Leipzig, A. Barth, 1908) has recently, as a result of a noteworthy series of studies, elaborated a really illuminating theory of agglutination, satisfactory both from a chemical and a biologic point of view. This theory attributes agglutination to a specific precipitin reaction, as Paltauf had already assumed. The formation of a precipitate through the combined action of the typhoid serum and the typhoid culture effects the phenomenon of clumping as a side issue, due to mechanical causes. Paltauf, in accord with the current theory of specific precipitins, assumes a precipitation of a specific constituent of the bacteria by its antibodies; van Calcar concludes that the substance precipitated is a globulin from the serum itself. The globulin precipitate, according to van Calcar, is due to the specific digestive ferments of the immune serum, which are called forth by the specific protein serving as the antigen. Consequently if the antigen-protein and the immune serum be brought together, the former is decomposed. The amino-acids resulting from this decomposition cause a precipitate of globulin, which is extremely sensitive to acids. In this reaction the globulin plays, as it were, merely the part of an indicator. According to this theory, the specificity of the reaction depends not upon a specific precipitin, but merely on the presence of that specific immune serum which decomposes the particular antigen, and thereby causes the precipitation of the globulin. Thus the agglutination reaction is identical with the specific precipitin reaction of the serum in infectious diseases first noted by Kraus. It is, however, much more easily detected, because a minimum, otherwise inappreciable, precipitate is rendered visible by the clumping of the bacteria.

[2] See Widal, Semaine médicale, 1896, No. 33, p. 259, and the numerous confirmatory results published in this journal of the same year. Also the contributions of German authors, in particular those of Stene, Centralbl. f. inn. Med., 1896, No. 49, and Breuer-Lichtheim, Berlin. klin. Woch., 1896, Nos. 47 and 48. Finally, Widal's chief work on the subject, M. F. Widal and M. A. Sicard, Annales de l'Institut Pasteur, 1897, vol. xi, No. 5.

would exert this action in order to consider the test positive for the diagnosis of typhoid.

Widal's reaction is performed quantitatively in the Bern Clinic as follows—a convenient and reliable method:[1] A barely turbid dilution of an actively motile twelve- to fifteen-hour agar culture of typhoid bacilli in sterile physiologic salt solution is used. This dilution is obtained by pouring the salt solution directly into the agar tube, shaking, and, if necessary, rubbing off a bit of the growth with a sterile platinum loop. If the mixture be too turbid, it may be partially cleared by filtration or centrifuging.

Two series of small glass dishes, A, B, C, D, and I, II, III, IV, V, are set out. (See Fig. 317.) The former are used in diluting the serum, which is performed as follows:

By means of a dropper, best made by drawing out a glass tube, one drop of the serum to be tested is placed in each of dishes A, B, and I. The dropper is then washed, and in A are placed 4, in B 9, drops of physiologic salt solution. This is mixed with the serum by means of a platinum loop. Thus we obtain in A a dilution of 1 : 5, in B one of 1 : 10. To make dilutions of 1 : 50 and 1 : 100 one drop of the mixture in B is mixed in C and in D with 4 and 9 drops respectively of physiologic salt solution. Thus in C there is a dilution of 1 : 50, in D one of 1 : 100. Higher dilutions may be made if desired in the same manner.

One drop each of dilutions A, B, C, and D is now placed in dishes II, III, IV, and V respectively. Between each transfer the pipet must be rinsed in water. In each of dishes I, II, III, IV, and V are then placed 9 drops of the suspension of bacilli, always using the same pipet, and a careful mixture is made by means of the sterile platinum loop, which is then immediately flamed. The addition of the emul-

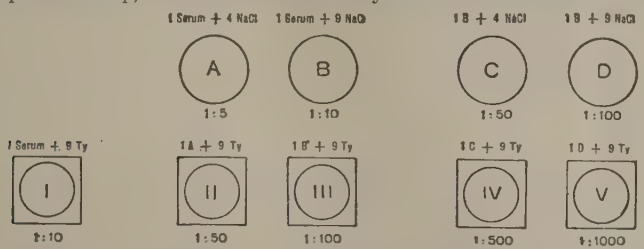


Fig. 317.—Manner of diluting the serum and arrangement of the dishes in the Gruber-Widal reaction.

sion of bacilli makes the dilutions ten times as high throughout, so that the final dilutions are I = 1 in 10, II = 1 in 50, III = 1 in 100, IV = 1 in 500, V = 1 in 1000. All the dishes contain the same amounts of serum dilution and bacteria.

From each dilution a fresh microscopic preparation is made by covering a drop placed on a slide with a cover-slip, under one edge of which a second cover-slip is placed. This insures a wedge-shaped layer of fluid of sufficient thickness and very convenient for examination. A little vaselin is smeared around the edges of the cover-slip in order to prevent evaporation, and the slide is kept at a temperature of 37° to 40° C.[2] Every half-hour they are examined for agglutination with a No. 7

[1] See M. von Wyss, Klinische Untersuchung über Erscheinungen von Agglutinationshemmung bei der Anstellung der Gruber-Widalschen Reaction, Inaug. Academ. Dissert., Bern, 1906.

[2] The assertion that the agglutinating power of the serum is strongest at a temperature of 50° to 55° C. has not been confirmed by recent studies. The question of the optimum temperature for the Widal reaction is much complicated by the presence in the serum of substances which hinder agglutination (p. 860); for it is quite conceivable that in case the influences favoring and those hindering agglutination be differently affected by temperature according to the proportions of the agglutinin and the substances hindering agglutination, the end-result may be influenced by the temperature in an apparently irregular way. Not only should all possible dilutions of the serum be examined, but these should be placed in different temperatures if one wish to be sure not to overlook any possible agglutination. One may conform to the condition "in different temperatures" if one use the remainder of the dilutions in the method described above for examination at ordinary temperatures. Many negative Widals may be explained by the complicated influence of dilution and temperature.

objective (Zeiss). All the apparatus, as well as the remaining culture, should be disinfected in bichlorid solution after use.

[A somewhat simpler and more convenient method than the above is as follows: Collect about 10 drops of blood in a small sterile test-tube and allow it to clot. Mix 1 loopful of the serum with 4 loopfuls of physiologic salt solution previously placed on a clean glass slide. This is dilution No. 1 (1 in 5). Mix 1 loopful of dilution No. 1 with 4 loopfuls of salt solution on a second slide. This is dilution No. 2 (1 in 25). Mix 1 loopful of dilution No. 2 with 1 loopful of salt solution on a third slide. This is dilution No. 3 (1 in 50). Now transfer 1 loopful of each of these dilutions to each of three clean cover-slips and add 1 loopful of a twelve- to eighteen-hour broth culture of Bacillus typhosus. The final dilutions are thus 1 in 10, 1 in 50, and 1 in 100. Finally, mix 1 loopful of the culture with 1 loopful of salt solution on a fourth cover-slip. This is the control. A hollow-ground glass slide rimmed with vaselin is then inverted upon each cover-slip, then turned right side up, and the hanging drop examined under the microscope. The capillary tubes employed by Wright in opsonic determinations may be employed to collect the blood, and, to one accustomed to their use, are more convenient and time saving.—Ed.]

In pronounced cases of typhoid the agglutinating action of the serum may be so marked that even with a dilution of 1 : 100 the typhoid bacilli will lose their power of motion and will adhere in clumps immediately after the addition of the serum. When the agglutination is less vigorous, the reaction may not be manifest for a considerable time, or it may occur only in the more concentrated dilutions. Before an absolute diagnosis of typhoid fever is made from the serum action alone, agglutination should take place within an hour with a dilution of the serum of 1 : 50. The sooner clumping occurs, the safer one is in expressing an opinion. The reaction should, however, be called positive for typhoid, even if (using a dilution of 1 : 50) complete agglutination occur in one to two hours.

Different typhoid cultures vary in their susceptibility to clumping, so that each observer should make himself familiar with the peculiarities of his own cultures. This explains many variable results reported.

In some cases of typhoid fever the reaction may be positive as early as the first week, but in most cases it may not be expected until the second or even the third week of the disease. Not uncommonly, however, the reaction is first positive in the fourth week or even during convalescence. In such cases its practical value is, of course, somewhat questionable. This is true even if one take into account the cessation of motility mentioned below, and is not misled thereby. The same statements apply to the disappearance of the reaction. This may occur a few weeks after the recession of the fever, but usually not for four to five months. Cases in which a positive Widal reaction can be obtained several years after recovery are rare, but to avoid mistakes it is important to remember that they do exist.

The supplementary demonstration of a positive reaction in the mildest or quite latent, unrecognized cases of typhoid (bacillus carriers) is of significance in explaining epidemics. By its aid the cause of the continuance of an epidemic and the common source of apparently isolated cases connected only by such a bacillus carrier may be established.[1]

The frequently observed positive Widal reaction in *icterus* is noteworthy. Since it is not constant, we cannot assume that it is caused by the bile in the blood. Direct experiment supports this statement. It may be that it occurs in cases of jaundice which are caused by bacteria related to typhoid bacilli, *i. e.*, belonging to the same group.

In this connection the author will record what he believes to be a new observation (first described by Grünbaum), made independently in his clinic during an epidemic of typhoid fever. Early in the disease the serum of the patients produces more marked agglutination in weaker than in stronger concentrations; but this condition is reversed during the course of the disease. This indicates that, in addition to the agglutinative effect of the serum, there is a counteraction against agglutination early in the disease, which may be overcome by the more marked dilutions. Ehrlich's school considers this due to the influence of an agglutinoid, *i. e.*, a substance resembling agglutinin in having a common origin and possessing the same "haptophore" group as it, and therefore possessing the same affinity for the typhoid bacilli, but which does not agglutinate because the "zymophore" group is different. If one assume that there is less agglutinoid in typhoid serum, but that it is more active than the agglutinin, one can understand how agglutination seems to be

[1] See Nägeli, Ueber die Typhus epidemie in Oberbipp, Correspondenzbl. f. Schweiz. Aerzte, 1899, No. 18.

arrested, because the agglutinoid, on account of its greater activity, combines with the protein of the bacilli, while this does not occur in less concentrated mixtures because of the dilution. This, of course, is directly opposed to van Calcar's theory of agglutination (p. 858, note 1). Further investigations must be undertaken in order to determine whether these differences between the effects of concentrated and dilute serum mixtures are of any value in predicting the clinical course of a case. So far as our experience goes at present this seems not to be the case. At all events, the observation is of practical importance, since it demonstrates that a negative result should never be assumed simply because agglutination is not obtained by a concentrated serum, but that an opinion should be withheld until the test has been made with a much diluted serum, for it has not yet been shown whether far higher dilutions than those usually employed have not certain advantages, or whether the influences inhibiting agglutination do not preponderate in the usual dilutions, and whether, therefore, many negative results may not be avoided by choosing still higher dilutions.

In order to have fresh typhoid cultures always on hand it is best to transfer the glycerin-agar cultures every eight or fourteen days, as otherwise the cultures will degenerate and die off. A fresh agar culture is prepared from the water of condensation of the agar culture twelve to fourteen hours before performing the test and placed in an incubator. Stock cultures, after being grown for a little while, are best preserved at the temperature of the room. Authentic typhoid cultures are best obtained from the spleen of a fresh typhoid corpse (with the ordinary precaution to avoid contamination, *i. e.*, singeing the surface).

Attempts have recently been made to substitute for the original Widal reaction analogous reactions with typhoid bacilli killed with formalin and preserved (Ficker's Diagnosticum [1]).

On the other hand, de Rossi [2] has found that typhoid (bouillon) cultures killed by exposure to 58° to 60° C. for one hour, are even more sensitive than fresh cultures. They may be kept for three months.

Krauss's precipitin reaction, obtained by mixing extract of typhoid bacilli and typhoid serum, has been recommended as a substitute for the Widal reaction. It obviates the use of living typhoid cultures, but it is less delicate than the agglutinin reaction. (See p. 858, note 1.)

The Gruber-Widal test has recently served to cause considerable confusion through the creation of the pathologic conception of paratyphoid. This term is used to designate certain forms of typhoid fever in which the Gruber-Widal test is negative with ordinary typhoid bacilli, whereas a positive reaction is obtained if a so-called paratyphoid culture be used. The paratyphoid bacillus is an organism obtained originally in diseases resembling typhoid fever in man, and distinguished from Bacillus typhosus by certain slight and by no means pronounced cultural differences. Serum from patients with paratyphoid is claimed to agglutinate the paratyphoid bacillus, just as that from patients with true typhoid agglutinates typhoid bacilli. Paratyphoid fever is said not to differ clinically from true typhoid, though the disease is usually milder, nor does autopsy show any pronounced differences, except that the abdominal lesions are less severe. Bacteriologists lay great stress on the fact that the paratyphoid bacillus, in contrast to Bacillus typhosus, is markedly pathogenic for mice and guinea-pigs, and that even small subcutaneous doses cause septicemia and death. These reasons seem to the author to be insufficient to warrant the establishment of paratyphoid fever as an independent and specifically distinct disease. To him it appears doubtful if the two diseases can be certainly distinguished clinically or anatomically. Moreover, the bacteriologic characteristics themselves vary so that even among paratyphoid bacilli many varieties have been isolated.[3] Further, the agglutination phenomena of the two so-called varieties permit of no sharp differentiation, since up to a certain degree, *i. e.*, within certain limits of dilution, the typhoid bacillus is agglutinated by paratyphoid serum, and vice versâ, while the typhoid serum sometimes fails to agglutinate the Bacillus typhosus, and paratyphoid serum fails to clump the paratyphoid bacilli. These should be logically sufficient grounds for protesting against the attempt to class typhoid and paratyphoid as two essentially different maladies. The author

[1] Furnished with directions for use by Merck in Darmstadt. More recently a similarly made paratyphoid "diagnosticum" has been prepared. In regard to the importance of the diagnosis of paratyphoid see below.

[2] Centralbl. f. Bact., first part, vol. xl, pp. 426–430.

[3] See Kolle, Die experimentelle Bakteriologie der Infectionskrankheiten, second ed., Wien, 1908, p. 222, et seq.

can hardly understand the ready acceptance of this distinction by certain clinicians. We know, from a thousand examples in the bacteriology and experimental pathology of infectious diseases, how markedly the characteristics of a bacterium may vary under different nutritional conditions in artificial culture-media, as well as in the body, how not merely the morphology, but also the virulence and the chemical properties of a particular species, can be changed because of its adaptation to certain conditions of life. Typhoid and paratyphoid bacilli then are apparently only different varieties, not different species. The only satisfactory explanation of the variations is that they result from natural selection, because the typhoid bacillus can assume different characteristics depending on the varying susceptibility of the chemically different soil in the living body, and that these are retained, up to a certain degree, by succeeding generations without, as well as within, the infected organism. Characteristics resembling those of the paratyphoid bacillus, exhibited also by Bacillus typhosus as regards the peculiarities of agglutination, are not, therefore, in the author's opinion, intrinsic qualities of these germs, but are the products of natural selection in certain forms of the disease caused by the typhoid bacillus. This does not, of course, exclude the possibility that the bacilli generated in a given case of typhoid may retain their acquired characteristics to a certain degree in a number of subsequent generations. It should be remembered that individual epidemics of other infectious diseases, such as scarlet fever and measles, quite frequently present points of difference, though up to the present no one has subdivided them into new groups. It is true that an attempt at further subdivision has recently been made even here (the so-called "morbus tertius"), but it is hardly justifiable, because the transition forms are so apparent and because no bacteriologic data are available. An attempt to cross-breed paratyphoid and typhoid bacilli would be of interest. With just as much reason might we differentiate parapneumococci, paradiphtheria bacilli (as indeed has, in a sense, already been tried, the name pseudodiphtheria bacilli being used), parastaphylococci, parastreptococci, etc. Into what confusion would we thus be plunged and at what variance would such a tendency be with the aims of other departments of scientific botany! The author does not deny that the differences discovered between ordinary typhoid and paratyphoid bacilli possess a certain clinical interest, chiefly because a positive paratyphoid reaction enables one to recognize also those cases of typhoid which give a negative Widal reaction. He cannot, however, allow the right of bacteriology to introduce new diagnoses on the grounds of such indefinite and minute distinctions, thereby overstepping the boundary of an aid to clinical knowledge and attempting to rule the clinician.

In *tuberculosis* also an attempt has been made to obtain an agglutination of a homogeneous suspension of sterilized tubercle bacilli (to be obtained from the Höchst laboratories). This, however, has not proved to be of any practical value. The *agglutination test of Malta fever*, on the other hand, is useful. (See p. 813, et seq.)

EXAMINATION OF THE BACTERICIDAL POWER OF THE BLOOD

Hamburger[1] has shown that the bactericidal power of the serum depends in large measure upon its content of CO_2, because the degree of alkalinity also depends on this. In order, therefore, that the conditions of any test of the bactericidal power of the blood may correspond with those in the living body, the blood should be defibrinated, care being taken to prevent the introduction of any air. Hamburger accomplishes this by shaking the blood with glass beads in a closed vessel filled to the brim. As a matter of fact, this procedure is of no advantage, because large amounts of human blood can be obtained only by employing artificial venous stasis, as a result of which the CO_2 content is artificially increased by an unknown amount. It is, therefore, rather to be recommended that the blood be arterialized before the serum is expressed. This is most simply done by letting the blood flow in a thin stream along the side of the test-tube in which it is collected. One may then wait for spontaneous coagulation and draw off the serum expressed from the clot under aseptic precautions. Or one may defibrinate the blood by shaking it up with glass beads under aseptic precautions, avoiding the entrance of air, and may then centrifuge it or allow the red cells to settle. Hamburger places the serum so obtained in two sterile test-tubes, one of which is heated to 60° C. for ten minutes. Both tubes are then inoculated by means of a sterile capillary pipet with an equal amount of the particular bouillon culture to be tested. The amount of culture used must be so small that no appreciable turbidity results. The tubes

[1] Osmotischer Druck und Ionenlehre, 1902, vol. i, p. 282, et seq.

are then placed in the incubator, and the time at which the first sign of turbidity appears is noted. The difference in time between the appearance of turbidity in the two tubes is an approximate measure of the bactericidal or inhibitory action in the unheated serum. According to Hamburger, when turbidity has appeared in the tubes, equal amounts of the fluid may be placed in narrow tubes (Fig. 305, p. 767), centrifuged, and the height of the sediment measured. It is well, however, in either case to make sure, by microscopic examination of dried smears, that the turbidity depends essentially on the bacteria and not on an amorphous protein precipitate, for in the latter case the method is unreliable. Hamburger recommends both methods, by means of which he studied the influence of CO_2 in the blood on the bactericidal power of the blood-serum. Very unreliable results had been obtained by him with the customary counting method by means of agar plates. The supposition that in this method the germs can be completely isolated from one another by mixing the serum with the melted agar is not warranted by facts.

THE WASSERMANN-NEISSER-BRUCK SERUM-REACTION IN SYPHILIS

In the diagnosis of doubtful cases of syphilis we must, in addition to the demonstration of the Spirochæta pallida (p. 815, et seq.), consider the so-called serum-reaction of Wassermann, Neisser, and Bruck. It is of considerable importance, from the point of view of therapy, not only in detecting cases of visceral syphilis, but also in determining the etiology of cases of tabes dorsalis and general paresis, because it is positive in a relatively high percentage of these cases.

This so-called serum reaction depends on the deviation of the complement, a method introduced by Bordet and Gengou. These writers have shown the existence of characteristic chemical affinities between the antigen and the corresponding amboceptor. It is by means of these affinities that the demonstration of the amboceptor by means of its corresponding antigen and vice versâ is possible. We know that by injecting the blood-cells of any particular species of animal into an individual of another species we may obtain from the blood of the latter a sort of immune serum which contains a specific amboceptor or immune body against the cells used for the injection. The action of this amboceptor, *i. e.*, of the particular antiserum, is shown by its dissolving in vitro the kind of corpuscles used, in case the mixture contain at the same time the so-called complement that puzzling substance present in every normal serum, and called the alexin by the French school. After a rabbit has been inoculated with sheep's blood, its serum contains a specific immune body, which in the test-tube dissolves sheep's corpuscles in the presence of the complement. If the rabbit serum be fresh, it contains the complement itself. Heating and aging of the serum destroy the complement, and it is, therefore, necessary, in order to re-establish the hemolytic action, to add the complement in the form of fresh serum from some animal or other, for instance, the fresh serum of a normal guinea-pig. Such a combination of blood-corpuscles, amboceptor, and complement is usually called a specific hemolytic mixture. According to Ehrlich, the hemolytic effect results from the fact that the amboceptor, serving to some extent as a linking body, anchors the complement to the red cells, thus enabling it to dissolve them. In such an experiment the red cells play the part of antigen to the hemolytic amboceptor, *i. e.*, the same part as that played by the bacteria to their specific antibodies in bacteriolytic experiments. The complement is essential to the success of the experiment, and it follows from this that a mixture of blood-corpuscles and the particular specific hemolytic amboceptor may be utilized as an indicator of the presence of the complement. If free complement be present, hemolysis occurs; if it be lacking, there is no hemolysis. If now there be added to the hemolytic mixture some other "foreign" amboceptor and its corresponding antigen, we have present in the mixture two amboceptors with their corresponding antigens beside the complement. There then begins a kind of contest between the two amboceptor-antigen groups for the complement, and if certain mass relations obtain, the complement will be so far deviated to the "foreign" amboceptor which has been added to the hemolytic mixture, *i. e.*, anchored to the corresponding antigen, that (in the presence of the proper proportions) the complement requisite for hemolysis is lacking and, therefore, the hemolysis itself either fails or is at least retarded. The test is still more accurate if the "foreign" amboceptor, its antigen, and the complement be first mixed together, allowed to stand a while, and, then, after union of these three substances, the blood-corpuscles with their specific hemolytic amboceptor be added. The result of this Bordet-Gengou test is called arrest of hemolysis by deviation of the complement.

By means of this procedure the etiologic significance of certain bacteria in infectious diseases, *e. g.*, that of Bordet's bacillus in whooping-cough (p. 720) and Kruse's

bacillus in dysentery (p. 530, et seq.), may be shown. Wassermann uses it as an aid in diagnosis to demonstrate either syphilitic antigen (the poison of syphilis) or syphilitic antibodies, both of which may be present in syphilitic organisms. Usually the practical diagnosis of syphilis depends on the demonstration of syphilitic antibodies. One must have at hand for this demonstration the ingredients needed in an ordinary test for specific hemolysis, *e. g.*, sheep's red cells, amboceptor from rabbits immunized against these, and fresh guinea-pig serum containing the complement, beside the syphilitic antigen, *e. g.*, an extract of the liver of a syphilitic fetus. With these is sought the syphilitic amboceptor or immune body, which may be present in the blood-serum and even in the cerebrospinal and other body fluids of the person examined. The rabbit serum containing sheep amboceptors and the human serum to be examined must be deactivated, *i. e.*, freed from complement. The object of this is to use a same amount of complement in all the tests in spite of the different additional amounts of hemolytic amboceptor and of the serum to be tested. The technic of the Wassermann-Bruck-Neisser test (omitting the complete details of the procedure to be given later) is as follows: For a few weeks a rabbit is injected at definite intervals with a definite amount of sheep's red cells, and the serum obtained from it is deactivated by heating to 56° C. for a definite time. Rabbit serum so treated contains the hemolytic amboceptor. Fresh guinea-pig serum is also procured. Syphilitic amboceptor in the form of an extract of the liver of a syphilitic fetus is now mixed in a test-tube with the human serum to be tested and with complement in the form of fresh normal guinea-pig serum, to which are added sheep's blood-cells and the corresponding amboceptor. The exact proportions of the ingredients used are given below The entire mixture is then kept at 37° C. for one or two hours. If the serum tested contain syphilitic amboceptor, hemolysis either fails entirely or is much delayed, because the complement necessary for hemolysis is taken up.

The following are the detailed directions worked out in Neisser's clinic and formulated by Tage (Münch. med. Woch., 1908, No. 23).

1. *Obtaining the Substances Necessary for Reaction.*—The syphilitic antigen is obtained by finely dividing the liver of a syphilitic fetus, adding ten times its volume of absolute alcohol, shaking it up with powdered glass in a shaking apparatus for twenty-four hours, and filtering.

2. *Obtaining the Sheep's Blood-corpuscles.*—Fresh sheep's blood is defibrinated at the slaughter-house by shaking it up with steel shavings. Blood so defibrinated may be preserved for several days in the ice-box. For use, the necessary amount is washed twice with a double quantity of salt solution in the centrifuge and the water used for washing is pipeted off, so that there remains a pulpy mass of corpuscles mixed with a little salt solution.

3. *Obtaining the Amboceptor for the Red Cells.*—Into the ear vein of a large rabbit ½ cc. of the sheep corpuscle suspension is slowly injected. This is repeated four times at intervals of one week, and after five weeks have elapsed the animal is bled to death from the carotid. In order to obtain as much blood as possible the animal's abdomen is compressed during the hemorrhage. The blood is allowed to stand in vessels stoppered with cotton-wool for two hours, when the blood-clot is separated from the sides of the vessel with a platinum wire, and after twelve hours the serum is poured off. This is deactivated by heating in the water-bath to 56° C. for a half-hour; it is dried in vacuo at a temperature of 40° C., and portions of 0.3 gm. each of the residue are transferred to brown glass tubes in which it is kept for future use. For use 0.3 gm. of the dried residue is dissolved in 3 cc. of distilled water.

4. *Obtaining the Complement.*—A guinea-pig which has fasted for a day in order to assure bacteria-free serum is bled, and the fresh serum with complement contained in it is obtained in the same way as the amboceptor from the rabbit. This must be freshly prepared for each test.

5. *Obtaining the Fluid to be Examined.*—About 20 cc. of blood is withdrawn from a vein of the patient to be examined (p. 731), allowed to clot, and the serum obtained as in 3 and 4. If the cerebrospinal fluid is to be used, it is withdrawn by lumbar puncture in the usual way (p. 937 et seq.). The serum as well as the cerebrospinal fluid is deactivated by heating to 56° C. for half an hour, thereby freeing it of complement, and preserved in the cold.

The complexity of the process for obtaining the substances necessary for the reaction, especially the syphilitic antigen and the blood-cell amboceptor, makes it desirable that these might be dispensed from some central station.

The Actual Technic of the Reaction.—The substances entering into consideration are always used in dilutions for which 0.85 per cent. salt solution is employed. For use, 1 cc. of the alcoholic extract of antigen is mixed with 3 cc. of salt solution; 1 cc.

of deactivated serum is mixed with 4 cc. of salt solution; 1 cc. guinea-pig serum is mixed with 9 cc. salt solution; 1 cc. of the amboceptor powder solution (0.3 in 3 cc. distilled water, see above) with 60 cc. salt solution; and finally 1 cc. sheep's blood-corpuscles "broth" with 19 cc. salt solution. These dilutions are always meant in the following directions concerning quantities of the amboceptor, complement, etc., used in the tests.

Preliminary Examination of the Individual Ingredients.—One cc. of the dilution of sheep's blood-cells, mentioned above, when mixed with 4 cc. salt solution, should show no trace of hemolysis on fifteen minutes' standing at incubator temperature; 1 cc. of the dilution of sheep's cells + 1 cc. of the dilution of complement + 1 cc. amboceptor dilution must give a clear solution in fifteen minutes at 37° C.; 1 cc. of the dilution of sheep's blood-cells + 1 cc. complement dilution + ½ cc. amboceptor dilution should cause solution in half an hour; 1 cc. sheep's blood-cells + 1 cc. complement dilution + ⅓ to ½ cc. amboceptor dilution, in thirty to forty minutes; and the same quantity of the first two substances with ¼ to ⅙ cc. amboceptor dilution in two hours. Should hemolysis occur too quickly in this preliminary test, the amboceptor dilution must be further diluted with an equal volume of salt solution. If it occur too slowly, the amboceptor powder solution must, on the contrary, be made stronger, 0.2 cc. instead of 0.1 cc. of the amboceptor powder solution being used in 60 cc. salt solution. In this preliminary test the mixture must always be brought up to 3 cc. by the addition of salt solution in order that the results may be compared.

It must further be determined as a control of the diagnostic test whether or not the antigen of itself alone (without antibody) or the antibody (serum) alone (without antigen) arrests hemolysis, for this sometimes happens. To this end two tests are to be made:

1. Two cc. antigen dilution + 1 cc. sheep's blood-cell amboceptor dilution + 1 cc. sheep's cells diluted + 1 cc. complement.

2. Two cc. of the serum to be tested + 1 cc. of dilution of blood-cell amboceptor + 1 cc. dilution of sheep's cells + 1 cc. complement. In both these tests uniform hemolysis must occur; if not, the antigen of itself or the antibody of itself (serum) has an influence in arresting the solution.

The Examination Proper.—This includes the following separate tests,[1] eight in number:

Test-tube 1 contains 1 cc. sheep's blood + 4 cc. physiologic salt solution.

Test-tube 2 contains 1 cc. complement + 1 cc. sheep's blood + 1 cc. amboceptor + 2 cc. salt solution.

Test-tube 3 contains 1 cc. normal serum + 1 cc. antigen + 1 cc. complement + 1 cc. sheep's blood + 1 cc. amboceptor.

Test-tube 4 contains 1 cc. syphilitic serum (for comparison) + 1 cc. antigen + 1 cc. complement + 1 cc. sheep's blood + 1 cc. amboceptor.

Test-tube 5 contains no serum + 2 cc. antigen + 2 cc. complement + 1 cc. sheep's blood + 1 cc. amboceptor. (This test has already been mentioned as a preliminary test.)

Test-tube 6 contains 1 cc. of the serum to be examined + 1 cc. antigen + 1 cc. complement + 1 cc. sheep's blood + 1 cc. amboceptor.

Test-tube 7 contains ½ cc. of the serum to be examined + ½ cc. antigen + 1 cc. complement + 1 cc. of sheep's blood + 1 cc. amboceptor + 1 cc. salt solution.

Test-tube 8 contains 2 cc. of the serum to be examined + no antigen + 1 cc. complement + 1 cc. sheep's blood + 1 cc. amboceptor. (This test also has been described as preliminary trial.)

Bruck recommends that in tests 3 to 8 the mixture containing the first 3 ingredients be kept in the incubator for one hour in order that the complement may be fully bound before the sheep's blood and the amboceptor are added. He likewise advises that the mixture of sheep's blood and the amboceptor be kept warm for one hour by itself. Not until then should all be mixed together.

The result of the different tests may be read after the tubes have been in the incubator for one hour. For a positive diagnosis of syphilitic antibodies in the serum tested, hemolysis must be absolutely lacking in tests 6 and 7, in which the serum tested and the antigen are present; and in tests 4 (containing serum known to be syphilitic) and 1, whereas in tests 2, 3, and 5 hemolysis must occur. Comparison with the test containing known syphilitic serum can be made to decide the question of a doubtful reaction (slight hemolysis).

[1] The author would again emphasize that the quantities refer to the dilutions mentioned above. Sheep's blood always means the given dilution of sheep's blood-cell "broth," etc.

Contrary to the whole basic idea of the method and to the nomenclature of the active substance contained in syphilitic serum (which has been retained above for better understanding), the Wassermann-Neisser-Bruck reaction has not proved itself to be strictly specific, *i. e.*, is not a specific test of the syphilitic antibody. For it seems that extract of guinea-pig's heart may be used with almost the same results as syphilitic antigen. Although this necessarily gives rise to grave doubts in the judicial mind of the critical observer as to the diagnostic significance of the reaction, nevertheless the reaction has made good and become established on purely empirical grounds. The few cases in which a positive reaction is obtained in spite of the fact that syphilis is absolutely excluded (scarlet fever) are practically of no moment, since the reaction soon becomes negative after recovery. Many workers actually use extract of guinea-pig's heart instead of syphilitic antigen, because the latter is so difficult to obtain. In consideration of this most striking fact the proposition has been made, and very properly, to represent this serum reaction in syphilis not as "specific," but merely as "characteristic" of the disease.

The varied modifications of Wassermann's technic chiefly concern the preparation of antigen. Marie and Levaditi[1] mash the liver of a congenitally syphilitic fetus in vacuo, pulverize it, extract in physiologic salt solution, centrifugalize, and use the supernatant fluid. Morgenroth and Sterz[2] preserve the syphilitic liver in the frozen state and use a small piece of it for each test. This bit is mashed in sea-sand, extracted in salt solution, filtered, and the filtrate used. Porgos and Meier[3] extract in alcohol, filter, evaporate the filtrate in a vacuum below 40° C., and use a 1 per cent. solution of the resulting sticky mass. Landsteiner, Müller, and Pötzl[4] make use of an extract of guinea-pig's heart or liver. Michaelis and Lesser[5] shake and extract minced normal or syphilitic liver or normal heart with alcohol and use 1 part of the clear supernatant fluid in 4 parts of physiologic salt solution. Sachs and Rondoni[6] use the following artificial antigen:

Sodium oleate (Kahlbaum)	2.5	or	1.0;
Lecithin (Ovo, Merck)	2.5	or	1.0;
Oleic acid (Kahlbaum)	0.75	or	1.5;
Distilled water	12.5	or	5.0;
Alcohol	ad. 1000.0	or	1000.0.

One part of the above is diluted with 5 parts of physiologic salt solution.

Schürmann prepares the following:

Lecithin	0.3 in 50 cc. absolute alcohol;
Sodium glycerophosphite	0.3 in 5 cc. physiologic salt solution.

Thirty cc. of the above are mixed with 5 cc. lactic acid and 10 cc. of a 1 per cent. solution of ammonium vanadinate.

NOGUCHI'S MODIFICATION OF THE WASSERMANN REACTION

Noguchi has considerably simplified the Wassermann reaction by using for reagents separate slips of filter-paper impregnated with complement, antigen, and amboceptor respectively, dried and standardized. His technic is as follows:

Reagents.—1. *Antihuman hemolytic amboceptor* is prepared in rabbits by injecting five or six times into the peritoneal cavity increasing doses (up to 20 cc.) of thoroughly washed human blood-cells at five or six days intervals. The blood of the rabbit is collected nine or ten days after the last injection and the serum allowed to separate. Either this serum or slips of filter-paper impregnated with it, dried and standardized, may be used.

2. *Complement* is fresh guinea-pig's serum, or slips of paper impregnated with the same, dried quickly at low temperature, and standardized.

3. *Antigen* is the acetone-insoluble lipoids of the organs; 1 part of the mashed tissue (liver, heart, or kidney of man, ox, dog, guinea-pig, or rabbit) is extracted with 10 parts of absolute alcohol for several days at 37° C., filtered through paper, and dried at a temperature below 40° C. by means of an electric-fan. The resulting

[1] Ann. Inst. Pasteur, 1907, vol. xxi, 138.
[2] Virch. Arch. f. path. Anat., 1907, vol. clxxxvii, 166.
[3] Kraus-Levaditi's Handbuch der Immunitätsforschung, 1909, vol. ii, 1182.
[4] Wein. klin. Woch., 1907, vol. xx, 1421 and 1565.
[5] Berlin. klin. Woch., 1908, vol. xlv, 301.
[6] Ibid., vol. xlv.

residue is extracted with ether, which is then allowed to evaporate. The residue from this is taken up with a small amount of ether and fractionated with 10 volumes of acetone. For the test the adequate quantity of a 0.2 per cent. emulsion of the residue (acetone-insoluble) after evaporation of the acetone in physiologic salt solution is used, or slips of filter-paper impregnated with an ethereal solution of the material may be employed.

4. *The suspension of human blood-corpuscles* is prepared by allowing 2 drops of blood from a normal individual to fall into 8 cc. of physiologic salt solution and then removing the fibrin by washing the corpuscles or by beating the suspension with a stick. It is more accurate to use a 1 per cent. suspension of the washed corpuscles, which is prepared by mixing the washed corpuscles from 1 volume of blood with 99 volumes of physiologic salt solution (but not 1 volume of the sedimented corpuscle mass to 99 volumes of saline).

5. *Serum to be Tested.*—About 1 or 2 cc. of blood from the patient are collected in a Wright tube. The clear serum which separates from the clot is used. No preliminary inactivation of the serum at 55° C. is required, unless the serum has been kept for several days after taking.

Six tests are made according to the following scheme:

	Test for diagnosis with the serum in question.	First control. Test with known syphilitic serum (positive reaction).	Second control. Test with normal serum (negative reaction).
Control tube without antigen for each test.	*a.* Patient's serum, 1 drop.[1] (1) *b.* Human blood suspension, 1 cc. *c.* Complement, 2 units.[2]	*a′.* Positive luetic serum, 1 drop. (3) *b′.* Human blood suspension, 1 cc. *c′.* Complement, 2 units.	*a″.* Normal serum, 1 drop. (5) *b″.* Human blood suspension, 1 cc. *c″.* Complement, 2 units.
Determinative tube containing antigen.	*a.* *b.* (2) *c.* } do. *d.* Antigen.	*a′.* *b′.* (4) *c′.* } do. *d′.* Antigen.	*a″.* *b″.* (6) *c″.* } do. *d″.* Antigen.

Incubate at 37° C. one hour.
Antihuman hemolytic amboceptor, 2 units[3] to all tubes, 37° C. for two hours longer. Then at room temperature.

Reading the Reaction.—A negative reaction is shown by complete hemolysis in both tubes containing patient's serum irrespective of the presence of antigen. This usually occurs in one hour or less. A positive reaction is shown by complete absence or partial inhibition of hemolysis in the tube containing antigen, and complete hemolysis in the tube without antigen. Tubes 1, 3, 5, and 6, therefore, should all show complete hemolysis before the final reading of the reaction.

Results of the Noguchi Test.—In 1082 cases of syphilis, parasyphilis, hereditary syphilis, and suspected syphilis Noguchi's test was positive in 802, or 74 per cent. Of these, 39 had been under prolonged treatment for the disease and only 10.2 per cent. of them gave positive reactions. Noguchi's test is somewhat more frequently positive than Wassermann's reaction. Thus, in 244 cases of syphilis Noguchi's test was positive in 211 (86.4 per cent.), whereas Wassermann's reaction was positive in only 183 (75 per cent.). In 333 cases where syphilis could be excluded with a fair degree of certainty Noguchi's test was positive in 13 (3.9 per cent.). Treatment for syphilis has a marked influence in reducing the number and intensity of positive reactions. It is fair to say that a positive Noguchi reaction is strong presumptive evidence of syphilis and an absolute indication for specific treatment.

Dr. Noguchi has been kind enough to revise the above note and also the note upon his butyric acid reaction on p. 941. During the past eight months Dr. Noguchi has examined for me 105 specimens of blood carefully selected from my

[1] When working with inactivated serum (*i. e.*, one from which complement has been removed by heating to 55° C.), 4 drops (0.08 cc.) should be employed.

[2] Either 0.1 cc. of a 40 per cent. solution of guinea-pig serum in salt solution or a slip of filter-paper containing 2 units of complement. A unit of complement is the smallest amount necessary to produce complete hemolysis with 1 unit of amboceptor.

[3] A unit of amboceptor is the smallest amount necessary to produce complete hemolysis in a standard suspension of erythrocytes in the presence of an excess of complement (usually 0.02 cc. of guinea-pig's serum is taken as 1 complement unit).

services at the New York City and the French hospitals, and a few from other sources. In this series of cases were included many types of arteriosclerosis, nephritis, anemia, myocarditis, hepatitis, two cases of trichinosis, one of severe epidemic parotitis accompanied by severe stomatitis, and many other acute and chronic diseases.

In only one instance was there any question of a positive reaction when the results of treatment, the clinical diagnosis, the history of the subsequent course of the disease, did not prove its accuracy. Twenty of the cases which gave a negative reaction had almost certainly suffered from syphilis. Some of them had been under specific treatment to a slight extent shortly before the reaction was made. The others did not show any especial clinical improvement attributable to the institution of specific treatment. A careful study of these results has convinced me that a positive reaction, even though it be a weak one, is from the therapeutic standpoint a very important aid in diagnosis. If the blood exhibit a negative reaction, it should be tested again at a later interval. In 2 instances in this series of 20 negative cases the subsequent examination became positive.—Ed.]

EXAMINATION OF THE MOUTH AND PHARYNX

Inspection is the most important method for examining the mouth and pharynx. For proper inspection the patient should open his mouth as wide as possible, and then move the tongue away from the place to be examined. The pharynx and soft palate are usually seen best if the base of the unprotruded tongue be depressed with a spatula or with the handle of a spoon, while the examiner steadies the patient's head at the same time with his other hand. Care must be taken not to apply the tongue-depressor too far back, for if the posterior portion of the base of the tongue or the pharynx be touched, gagging results and renders the examination difficult. The posterior wall of the pharynx can be seen better when the patient says "Ah!" and so elevates the soft palate. It is often very difficult, indeed, to examine the mouths of unruly children or of irrational patients. Sometimes closing the nostrils will make such patients open the mouth, while at other times we have forcibly to separate the jaws with a spoon, a depressor, or a mouth-gag. With unruly children, whether we employ the aid of a depressor or not, we should look quickly the moment the child opens his mouth to cry.

Palpation with the finger often assists in determining the condition of portions of the mouth which are situated farther back. Palpation of the nasopharynx or of the entrance to the esophagus to hunt for foreign bodies, retropharyngeal abscesses, or adenoids must be done very quickly, because it is extremely disagreeable to the patient and can be borne but a short time.[1] Unruly patients and children are apt to bite the examiner's finger unless the cheek is pressed in between the patient's teeth with the free hand. This is a better method than to employ appliances for protecting the fingers. The forefinger is better adapted for palpating adults, and the little finger for very young children. The introduced finger is hooked upward or downward, according to the region to be explored. The entire pharyngeal cavity can be palpated from the top of the larynx to the nasopharyngeal space above.

[1] [The application of a solution of cocain (2 to 4 per cent.) to the back of the pharynx will deaden the sensibility of the parts and allow a more careful digital examination.—Ed.]

Such palpation must be carried out very quickly because of the discomfort occasioned by it and the danger of causing vomiting. The most important use of this procedure is the diagnosis of adenoid vegetations, and such other methods as posterior rhinoscopy (p. 905), or

Fig. 318.

Fig. 319.

Fig. 318.—Hutchinson's teeth in hereditary syphilis: Two upper middle incisors (second dentition) with deep transverse and longitudinal grooves; also concave edge of middle incisors. The length of the teeth is normal, but the width is diminished; hence, broad interspace in middle.

Fig. 319.—Upper middle incisors (second dentition) immediately after eruption; also four lower incisors. Lower surface of upper incisors is rough, due to prominent points of dentin. Upper teeth short and directed away from each other, forming a broad interspace. On the four lower teeth are numerous excrescences, due to deficient formation of enamel. Base of excrescences everywhere at same level.

Lindt's direct rhinopharyngoscopy, can serve only as partial substitutes for it in the examination of adults and of older children. To carry out such palpation the examiner should stand to the right of and

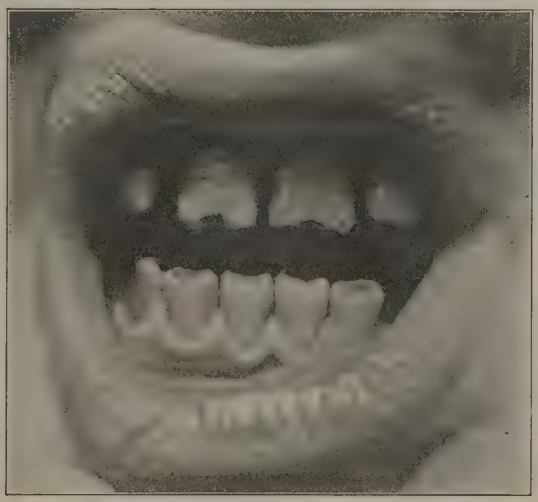


Fig. 320.—Hutchinson's teeth: The upper middle incisors (second dentition) and all four lower incisors are characteristic enough. The photograph was taken from a colored child, six years of age, who had been under Dr. McConnell's observation at the Vanderbilt Clinic for a year. She has saber shins, and when first brought to the clinic, presented a rash. An older sister has similar teeth. The mother has had two miscarriages since the birth of her last child. The original of this photograph has improved upon biniodid of mercury.

somewhat behind the patient, adults being seated in a chair, while children are best held in the lap of an assistant; he then steadies the patient's head by pressing it against his own chest, pushes the patient's cheeks between the teeth in the manner described above, in order to escape

being bitten, and rapidly introduces his index-finger, or in the case of children his little finger hooked upward, following closely the middle line of the mouth until the posterior pharyngeal wall is reached; the finger is then made to follow rapidly along the pharyngeal wall into the retropharyngeal space, first in the direction of the vomer and then toward the roof of the pharynx. He then rapidly palpates the posterior nares, the roof, and the lateral walls of the space, and especially the Eustachian prominences. To reach and properly palpate the left lateral wall of the rhinopharynx from the right side, the examiner must rapidly move over to the other side of the patient, at the same time slightly withdrawing his finger. If large adenoid growths be present, the whole retropharyngeal space is found to be filled with a soft mass, in consistence like a knot of earth-worms, which prevents palpating upward behind the uvula. If the adenoid growth be smaller, the retro-

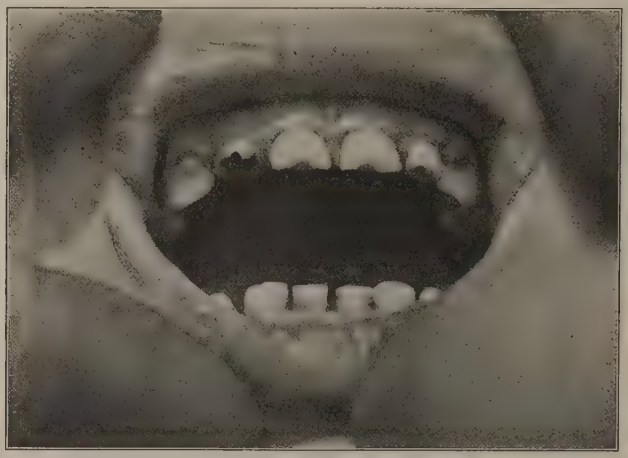


Fig. 321.—All four upper incisors approach the type of Hutchinson's teeth. The lower incisors are practically normal. In this case the upper middle incisors are not characteristically peg-shaped, but the groove upon the cutting edge is a significant feature. No other facts relating to this case are known. It is probable that the teeth should be classified as Hutchinson's teeth.

pharyngeal space is found to be more or less patent, and a soft mass is felt only by flexing the palpating finger upward toward the roof. The finger is often blood stained by the examination, for the vegetations are usually very vascular and easily injured. Palpation of the adenoid growths often gives better results than posterior rhinoscopy, because the latter is not only difficult, but also shows the vegetations very much foreshortened. Palpation must, however, be carried out very carefully, as it may easily cause injury.

Lips.—The examiner should notice their color (pallor, cyanosis), the presence of aphthous ulcers, mucous patches, sordes, fissures (rhagades) or their scars, which leave diverging folds at the corners of the mouth (children with hereditary syphilis), and herpes labialis. (See p. 66.)

Teeth.—The condition and the time of appearance of the first and second sets are important in childhood.[1] In adults we should

[1] [Note irregular dentition as indicating nasal deformity and former adenoids.—Ed.]

notice the state of preservation of the teeth. Poor teeth not infrequently cause digestive disturbances. They are quite commonly due to some general disturbance. Special attention should be paid to

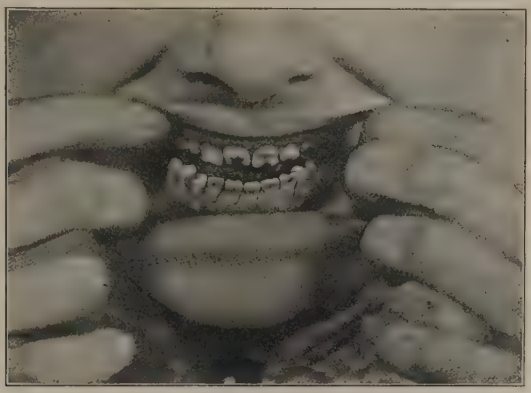


Fig. 322.—Irregular teeth simulating Hutchinson's teeth in a patient at the New York City Hospital, who exhibited at the time this photograph was taken a well-marked secondary syphilitic eruption.

so-called "rachitic teeth." They are characterized chiefly by transverse and longitudinal grooves with uneven enamel, which rapidly wears off

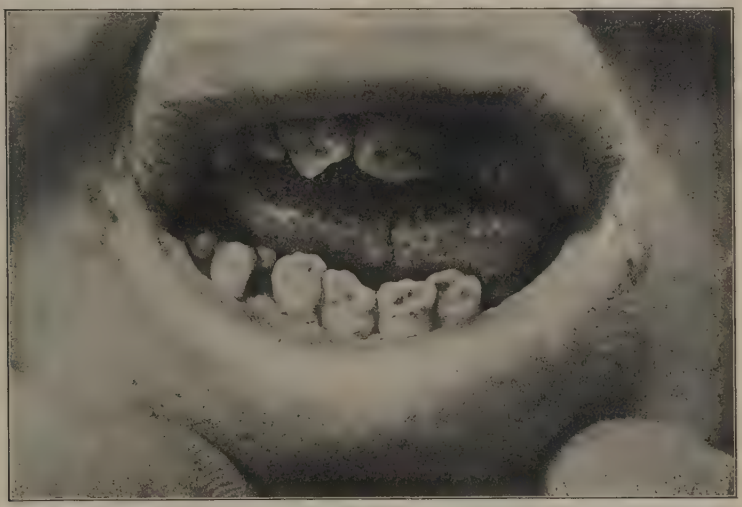


Fig. 323.—Irregular teeth in a young boy with a high arched palate. Although the two upper middle incisors are slightly wedge-shaped, there is not sufficient ground for considering them of the Hutchinson type. The irregularities are probably due to an inflammation of the gums during the second dentition (Dr. W. L. Stowell, Randall's Island Hospital).

on account of its irregular distribution. These changes are most marked in the incisors. In hereditary syphilis the teeth are often deformed, very much as in rachitis. Some of the dental deformities which are ob-

served in this disease are by no means characteristic of syphilis alone, but occur also in rachitis and other general disturbances, or even when the teeth-buds have been damaged by stomatitis. Hutchinson considers the type of teeth shown in Figs. 318 and 319 as pathognomonic of hereditary syphilis.[1] Other authors consider the concave notches in the

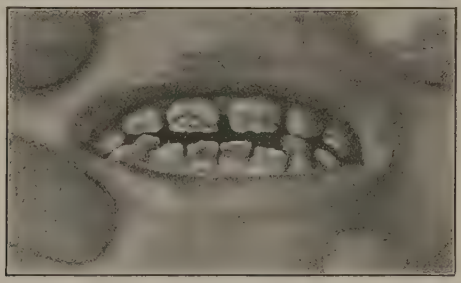


Fig. 324.—Irregular teeth, not Hutchinson's teeth (New York City Hospital).

lower margin of the upper middle incisors the characteristic feature (Fig. 318). The term "Hutchinson teeth" is applied more especially to those showing the latter peculiarity. These are observed chiefly in the second dentition. After the twenty-fifth year this concavity is usually worn away.

It is important to be familiar with the normal periods of the appearance of teeth, so as to be able to recognize anomalies in their appearance and to attach a

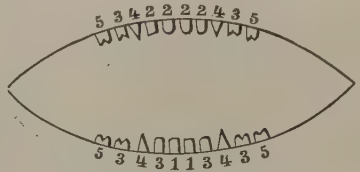


Fig. 325.—Sequences of teeth with first dentition (A. Vogel).

proper significance to the symptoms oftentimes connected with their eruption in early childhood.

A. Vogel makes the following statements (Fig. 325):

First Dentition.

First Group.—The two lower middle incisors appear almost simultaneously between the seventh and the ninth month.

Interval of three to nine weeks.

[1] ["Hutchinson's teeth" were first described in the Transactions of the Pathologic Society of London, July, 1858. In the original description he says: "There is a peculiar condition of the teeth resulting from hereditary syphilis, the most frequent conditions being the following:

"(*a*) *Smallness.*—They are small, stand apart, are rounded and peggy.

"(*b*) *Notching.*—They usually exhibit at the border a broad, shallow notch (sometimes two or three serrations).

"(*c*) *Color.*—They have a dirty-grayish surface without polish, and are rarely smooth.

"(*d*) *Wearing Down.*—They are deficient in enamel and are soft, and therefore liable to premature wearing down.

"(*e*) These signs almost exclusively apply to the incisors and canines."—Ed.]

Second Group.—The four upper incisors appear between the eighth and the ninth month, and follow one another rapidly within a few weeks, first the middle and then the lateral ones.

Interval of six to twelve weeks.

Third Group.—Six teeth appear almost at the same time between the twelfth and the fifteenth month. These are the first four molars and the two lower lateral incisors. Usually the anterior molars of the upper jaw appear first, then the lower lateral incisors, and finally the anterior lower molars.

Interval to the eighteenth month.

Fourth Group.—The four canines appear between the eighteenth and the twenty-fourth month.

Interval of two to three months.

Fifth Group.—The four second molars appear between the twentieth and the thirtieth month. This ends the first dentition, and the child then has the 20 "milk-teeth."

Second Dentition.

During this period the milk-teeth are supplanted by permanent teeth, and the three posterior molars in each jaw appear. The latter are not present during first dentition. A permanent set of 32 teeth then takes the place of the 20 milk-teeth. Second dentition begins in the fifth or sixth year of life, with the appearance of the first molar teeth in each side of the jaw. The milk-teeth now begin to fall out in the same order that they appeared. Each tooth as it falls out is supplanted immediately, or very soon, by the corresponding permanent tooth. The second molars appear during the twelfth year, and the third molars, or wisdom teeth, appear from the fifteenth to the twenty-fourth year, or sometimes still later.

Welcker's data differ somewhat from the above:

Table of Dentition According to Welcker.[1]

Teeth.	First dentition. Months.	Second dentition. Years.
Proximal incisors	6 to 8	8
Distal incisors	7 to 9	9
Canines	16 to 20	11 to 13
Proximal premolars	12 to 15	10
Distal premolars	20 to 24	11 to 15
First molars		7
Second molars		13 to 16
Wisdom teeth		18 to 20 to 30

Gums.—The gums are swollen and bleed easily in acute and chronic mercury-poisoning, occasionally after the use of iodids and bromids, in scurvy, and in other hemorrhagic conditions. Acute lymphoid leukemia is to be especially kept in mind. (See p. 835.) The bluish-gray "lead-line" on the gums, due to a deposit of lead sulphid in the mucous membrane, is of great diagnostic importance in chronic lead-poisoning. This line should not be confused with a discoloration of the teeth themselves at the junction of the gums. The latter is not uncommon in careless individuals and those who smoke a great deal. This discoloration is visible up to the margin of the gum, and may simulate the blue appearance of a lead-line very closely. It is quite easy to distinguish these conditions by pushing the corner of a stiff piece of paper beneath the margin of the gum. A true lead-line will become more distinct than ever, but the apparent lead-line, caused by the shining of the discolored teeth through the margins of the gums, will disappear entirely. A bluish discoloration, due to venous congestion, sometimes appears at the margin of the gums, not only in general circulatory disturbances, but in some local inflammations of the gums, and may lead to error. The pressure exerted by employing the piece of paper as above directed makes the gum anemic and renders the distinction easy.

[1] Arch. f. Anthropologie, 1866, vol. i.

Tongue.—The way the tongue is protruded at command is sometimes more or less characteristic. Very ill or stupefied patients protrude a tremulous tongue, and leave it out until told to withdraw it. Bites of the tongue [or their scars.—Ed.] are of great diagnostic importance in epilepsy.

We should examine the tongue of patients with bulbar symptoms closely for any noticeable atrophy. This atrophy may become quite marked indeed in progressive bulbar paralysis, and the tongue may exhibit pronounced fibrillary contractions. Many healthy individuals, however, present a slight fibrillary twitching of the tongue.

The so-called "coat" of the tongue, caused by hypertrophy and other changes of the epithelium that as yet have been but insufficiently studied, is of some diagnostic importance. The tongue is coated in all dyspeptic conditions and in fever. This coating is usually associated

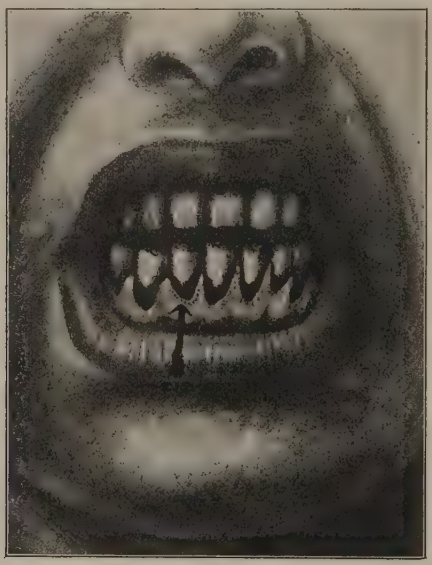


Fig. 326.—Lead-line: Note the interrupted, fringe-like line just at the edge of the gum (photographed from a water-color drawing) (kindness of Dr. R. C. Cabot).

with some disturbance in the appetite. Acute and chronic gastric catarrh is almost always associated with a coated tongue; but in ulcer of the stomach the tongue is often not coated, and there is no disturbance in the appetite. The causes of the epithelial changes leading to coating of the tongue are but little understood; there is, however, much evidence justifying the interpretations of the sign as a phenomenon of intoxication in the broadest sense of that word.

It is very often explained as being due to the fact that in people who do not eat, the lingual epithelium is not removed in a normal way by friction. This explanation, however, does not agree with clinical experience. Starvation does not result in a coated tongue.

According to L. Kurt,[1] this phenomenon appears in gastric disturbances in which he has demonstrated the return of food-elements from the stomach back to the mouth.

[1] Berlin. klin. Woch., 1906, No. 28.

Frequently in patients with high fever the tongue is not only coated, but dry, on account of the diminished secretion of saliva. Small fissures of mucous membrane are rather common in these cases and may cause some bleeding. The blood-crusts which form in this way, combined with the dried brownish epithelium of the tongue, produce a dark-brown or blackish, the so-called fuliginous, coat. This always indicates that the patient's condition is serious. It may be found on the lips at the same time.

The coating of the tongue is often stained by certain food-stuffs, drinks, or medicines (milk, red wine, coffee, cocoa, chocolate, licorice, [fruit, tobacco.—Ed.] etc.).

The presence of fungi must not be confused with an ordinary coating of the tongue. Fungi may be found on the tongue, as well as elsewhere on the mucous membrane of the mouth, and occur in the form of large thick patches. Fresh patches are easily recognized by their snow-white color and rounded outline. The older patches often lose this white color, and are of a peculiar dirty-gray appearance. The situation of these mycotic patches on the margin of the tongue, their appearance in other parts of the mouth, and their solid character distinguish them from a simple coated tongue. Fig. 291 represents the microscopic appearance of thrush.

The tongue should be examined for *aphthous patches* and *syphilitic sores*. The peculiar circular thickenings of the epithelium, with slight inflammatory signs, so-called "*leukoplakia buccalis*," must not be confounded with either of them. Leukoplakia, sometimes called "*psoriasis linguæ*," is much more extensive. Its nature is not as yet well known. In one such case the author found large numbers of pneumococci in the thickened epithelium. Whitish, thickened spots of epithelium, produced by the irritation of bad teeth or of too much smoking, may resemble syphilitic mucous patches very closely.

The nature of the so-called *black, hairy tongue* is utterly unknown.

The erythematous tongue of scarlet fever, with its red and swollen papillæ, is very characteristic. It is familiarly known as the "*strawberry* or *raspberry tongue*."

[Virchow's smooth atrophy of the base of the tongue[1] may be of some value in diagnosing late syphilis. It consists of an atrophy of the lingual tonsillar tissue, and can be appreciated by palpation better than by inspection.—Ed.]

Soft Palate; Tonsils; Pharynx.—The various kinds of acute angina are to be considered in this connection (*angina simplex, follicularis, necrotica, phlegmonosa,* and *diphtheritica*); furthermore, the different varieties of chronic pharyngitis (*pharyngitis sicca, granulosa,* etc.). (See text-books of Special Pathology.) In the author's clinic cases of diphtheria are examined according to the plan to be found in the appendix; this plan was likewise used in the diphtheria investigation carried out by the Swiss government.

Examination for Diphtheria Bacilli.—In doubtful diphtheric membranes only a microscopic demonstration of Löffler's bacilli (see Fig. 327) will prove the existence of true diphtheria. These bacilli are sometimes found in the membrane of true diphtheria in great numbers. Dry preparations may be made from the membrane in the same manner as described for the sputum, and then stained with the ordinary anilin stains, preferably by Gram's method. But cultures are generally

[1] Potter, Boston Med. and Surg. Jour., vol. cliv, No. 10, p. 260.

necessary. According to the investigations of the Bacteriologic Institute at Bern,[1] Löffler's horse-serum and glycerin-agar (7 per cent. glycerin) slants are the best media for growing diphtheria bacilli.

The media can be inoculated from the surface of the affected region of the pharynx by means of a sterile platinum loop [or a swab.—Ed.]. The round colonies of diphtheria bacilli, transparent at first, gradually become opaque. They may be seen after the tube has remained in an incubator about twelve hours. The colonies must be identified by preparing and examining microscopic slides, as macroscopically

Fig. 327.—Diphtheria bacilli (× 1000) (after Weichselbaum. Culture).

they may be confounded with those of other bacteria, especially streptococci. It is diagnostically important to remember that diphtheria bacilli are generally present in the pharynx in cases of laryngeal diphtheria, even when the pharynx itself is not visibly affected.

THE PRACTICAL VALUE OF THE BACTERIOLOGIC EXAMINATION FOR DIPHTHERIA

Diphtheria may be recognized clinically with a considerable degree of accuracy in the vast majority of cases, although demonstrating the presence of diphtheria bacilli may be very important.[2] Where there are clinical reasons for making a diagnosis of diphtheria (epidemics), we should not rely absolutely upon the result of a single negative bacteriologic examination (even when Löffler's modified serum is used). The author can cite numerous cases in which a single bacteriologic examination in the hands of experts was negative; yet diphtheria bacilli were discovered after repeated examinations and thus the early clinical diagnosis fully confirmed.

Negative results may easily be due to accidental conditions in inoculating the medium; or, in case the diagnosis is made to depend upon the result of cultures and the specimen is sent to a central laboratory, it must be remembered that the bacilli may have become less viable from drying. Again, other bacteria may easily outgrow the diphtheria bacilli in the culture-tube. The use of antiseptics (gargling, swabbing) in diphtheria is often responsible for a negative culture. Finally, for unknown reasons, certain diphtheria bacilli (discovered in the Bacteriologic Institute at Bern)[3]

[1] G. Michel, Das Wachsthum der Diphtheriebacillen auf verschiedenem Sera und Glycerinagar, I. D., Bern, 1897 (Centralbl. f. Bakteriologie). The writer concludes that Löffler's modified horse serum is the best medium of the five he examined, and that glycerin-agar is next. Löffler's ox serum and the pure ox or pure horse serum, without any addition, are considerably inferior. These results suggest that any statements in literature regarding false diphtheria are doubtful. Even the highly recommended Löffler's modified horse serum frequently gives a negative result, whereas, from the same case, diphtheria bacilli grew on one or the other inferior medium. Perhaps the most logical conclusion is that one negative examination does not prove anything.

[2] Deucher (Bern), Zur klin. Diagnose der Diphtherie, Correspondenzbl. f. Schweiz. Aerzte, 1895, No. 16, p. 485.

[3] Michel, *loc. cit.*

refuse to grow well upon the media which is generally supposed to be best. Allowances are not made for these circumstances (chances), and the capricious action of the diphtheria bacilli in the ordinary bacteriologic examination. Control examples have proved beyond doubt that these factors may influence the result of bacteriologic examination. A physician may err if he relies absolutely upon the bacteriologic examination, especially if attempted only once. Since the introduction of serum treatment this is a serious matter, from a therapeutic standpoint, and it may be still more disastrous from a prophylactic one.

A positive result, especially if results of cultures be exclusively depended upon, must also be carefully interpreted, for we know that virulent diphtheria bacilli are not infrequently found in perfectly healthy people, in ordinary cases of mild coryza and rhinitis, and in cases of pharyngitis which do not even produce a rise in temperature. It is hardly justifiable to administer antitoxic serum in these cases, because, as is well known, its use does not remove the bacilli. It is perfectly possible that at some later date a severe case of diphtheria may develop in the individual. *A logical and practical deduction is that the serum treatment should not be confined to cases where the bacteriologic examination is positive, but should be employed whenever the case presents a perfect clinical picture of diphtheria, or when there are severe symptoms and diphtheria bacilli are present in numbers, although the case may not resemble diphtheria clinically.*

The bacteriologic examination would be of much greater clinical value if in every case smears could be made directly from the pharynx, then fixed, stained, and examined under the microscope whether cultures are simultaneously made or not. The chief error in the modern culture method is that mere chance in inoculation may alter the results of cultures and the numeric relation of the bacteria, so that some species may be entirely suppressed. In one case the diphtheria bacilli may be overgrown by other bacteria and totally overlooked, and in another a few diphtheria bacilli may overgrow everything else, although in the actual illness they may be of little or no etiologic significance. In a dry preparation the conditions are represented as they actually exist. In the bacteriologic diagnosis of the upper air-passages, just as in the bacteriologic diagnosis of peritonitis of cystitis, culture results may be misleading so far as etiology of the affections is concerned. It seems probable to the writer that when dry preparations are granted their proper place in the diagnosis of angina, contradictions between clinical conditions and bacteriologic examinations will, for the most part, disappear. But the seat from which a dry preparation is made must be selected far more intelligently than in the present culture examination method—that is, when the diseased region is easily accessible, a slide must be prepared from it, and when diphtheria is in the larynx alone, more than the saliva must be examined. Especial attention should be paid to the tonsils and to the fossa between the pillars of the fauces. Sometimes it may be necessary to make several preparations, just as it is in the examination of sputum for tubercle bacilli. In making cultures, the importance of selecting the proper regions is often forgotten. In addition to the factors already mentioned, this neglect may explain the unsatisfactory lack of harmony between the clinical diagnosis and the bacteriologic examination. Dry preparations made from material sent for examination do not always fulfil the above demands, because the material may not be suited for microscopic examination.

The occurrence of diphtheria bacilli in the throats of healthy people or of those without clinical diphtheria or without croup has caused a great deal of confusion. The name pseudodiphtheria bacilli has been applied to such organisms. Morphologically they are quite similar to true diphtheria bacilli, that is, they show clubbed forms, have the same biologic and staining characteristics, etc., but do not possess the specific property of causing diphtheria, having been found in cases in which clinically no diphtheria was present. Every possible petty characteristic has been seized upon by which these bacilli could be distinguished from the true diphtheria bacilli in spite of the very great semblance between the two.

Virulence can be tested upon animals only after the bacteria have been altered biologically by making cultures. Hence it is clear *a priori* that animal experiments do not prove anything regarding the bacterial virulence in man. Besides, it has even been demonstrated that diphtheria bacilli taken from the buccal cavity of healthy people, although usually considered pseudodiphtheria bacilli, may sometimes be just as virulent for animals as true diphtheria bacilli taken from patients suffering from clinical diphtheria. The different influences of diphtheria serum upon animals inoculated with true and false diphtheria cannot be used as a differential point, because such a differentiation begs the question, taking it for granted that the cultures which act differently to the serum must of necessity belong to different

species. The numerous efforts[1] to separate the pseudodiphtheria bacilli from the true bacilli have been absolutely fruitless. It seems to the author better to assume that the variable significance of diphtheria bacilli for man is due to individual difference in species and to the continuous changes in varieties produced by repeated inoculations; and that such efforts to distinguish between true and false diphtheria bacilli by their morphology will probably never succeed.

Another point of distinction is the double stain recommended by M. Neisser.[2] He found that if dry specimens be prepared from a Löffler's serum culture ten to twenty hours old at 35° C., stained for one to three seconds with acetic acid-methylene blue,[3] washed in water, and then stained with aqueous Bismarck brown[4] for three to five seconds, certain isolated chromophilic portions of the organisms, the so-called polar bodies, stain blue. He claims that true diphtheria bacilli exhibited this peculiarity, but not the pseudobacilli.

This is in itself very interesting; but it is quite incomprehensible to the author that these writers fail to recognize that they argue in a circle in all these endeavors to discover points of differentiation between true and false diphtheria bacilli. Because the older differential characteristics have proved unreliable, they unconsciously fall back upon the clinical diagnosis by demanding that the true diphtheria bacilli must come from a case that is clinically diphtheria. Neisser's results, we believe, prove nothing more than that the polar stain is present in serum cultures made from clinical diphtheria, but is absent in cases which cannot be considered diphtheria from a clinical standpoint (healthy people, follicular tonsillitis, and doubtful clinical cases). According to the author's opinion, this peculiarity does not prove anything about the differentiation between true and false diphtheria bacilli, nor does it indicate the diagnosis in any given case. In typical cases there is no need of this criterion. The test does not decide whether these diphtheria bacilli, called false by Neisser, are anything more than varieties of so-called true diphtheric bacilli. Biologic variations responsible for the lack of a clinical picture of diphtheria may, of course, be equally responsible for the absence of his reaction. The cause of the variations may depend on the peculiarities of the medium or the suspectibility of the patient. Neisser considers his stain is available only for very young cultures upon Löffler's serum, which, of course, means that this criterion is not adapted to differentiate variations of species. The fact that this staining reaction is not trustworthy in dried preparations direct from the throat, and the emphasis placed upon the age of a culture, as well as the statement that false diphtheria bacilli, when old, may react in the same way, show how little value the method really has.

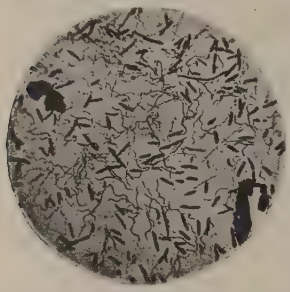


Fig. 328.—Dried smear of exudate in Vincent and Plaut's angina. Fusiform bacilli and spirocnætæ (× 500) (after Reiche).

Although the author does not consider the demonstration of Neisser's polar bodies sufficient for the differentiation between pseudodiphtheria bacilli and the true bacilli, yet he does not deny that these bodies are very valuable in differentiating morphologically diphtheria bacilli from other bacteria, much as the demonstration of capsules is of use in demonstrating penumococci. The latter demonstration, likewise, is not always successful.

Virulent diphtheria bacilli may be found in the fluids of the mouth months after the disease has run its course. Theoretically, this fact is very important for prophylaxis, but the practical difficulties are too great. In the first place, it would be almost impossible to isolate every convalescent from diphtheria until the throat examination was negative, and, in the second place, in view of the frequent occurrence of the diphtheria bacilli in healthy individuals' throats, such isolation would hardly be warranted.

The presence of streptococci and staphylococci is of interest in the etiologic study of different types of angina. They may often be present at the same time with

[1] See C. Fränkel, Die Unterscheidung der echten und falschen Diphtherie-bacillen, Berlin. klin. Woch., 1897, p. 1087, No. 50.

[2] Zeit. f. Hyg., 1897, vol. xxiv.

[3] One gm. of methylene-blue (Grübler) dissolved in 20 cc. of 96 per cent. alcohol, and then 950 cc. of distilled water and 50 cc. of glacial acetic acid added.

[4] 0.2 gm. Bismarck brown dissolved in 100 cc. boiling distilled water.

diphtheria bacilli (Figs. 281 and 285). Fränkel's pneumococcus (Fig. 281), the Micrococcus tetragenus (Fig. 287), the Micrococcus conglomeratus, and several others may also occur. Mention must be made of Bacillus fusiformis, which, together with a peculiar spirocheta, forms the bacteriologic characteristic of the so-called Vincent's or Plaut and Vincent's angina; this affection sometimes simulates diphtheria by the presence of a pseudomembrane; at other times is accompanied by the formation of ulcers. These organisms have not yet been grown in pure culture. The fusiform bacilli are gradually decolorized by Gram's method. The spirochetæ are Gram-negative.[1] All these bacteria frequently inhabit a normal mouth, so that little importance can be attached to their demonstration by culture methods as compared with the demonstration of their presence, in large numbers, in freshly prepared dry slides. (Regarding the method of preparation, see p. 715.)

THE DEMONSTRATION OF SPIROCHÆTA PALLIDA IN SYPHILITIC LESIONS

[The demonstration of Spirochæta pallida in syphilitic lesions of the mouth and pharynx, as well as of other parts of the body, may be mentioned here. The following is the technic of White and Avery,[2] using Schereschewsky's stain: The lesion is thoroughly cleansed by wiping with gauze. The junction of the necrotic and sound tissues, as well as a part of the floor of the ulcer, is then scraped with a small curet or scalpel until the superficial tissue is removed and a slight flow of blood is produced. The lesion is then sponged with dry gauze until the blood has ceased to flow and clear serum is seen to ooze. A drop of this serum is then spread on a perfectly clean glass slide in the thinnest possible uniform film. Smears so obtained are allowed to dry in the air and then passed through the flame three times. The staining fluid is freshly prepared by adding 13 drops (from a dropping-bottle) of Giemsa's solution (Grübler) to 10 cc. of a 0.5 per cent. watery glycerin solution. The mixture is then heated to boiling, immediately poured on the slide, and allowed to remain for from three to five minutes. The stain is then poured off and the slide washed with neutral distilled water. The slide is dried by shaking it rapidly through the air, and a second application of the stain is made for the same length of time. As a rule, two applications suffice to impart to the smear a distinct pinkish tinge. Should the pink be too faint, a third application is made. When the desired shade is reached, the slide is washed as above and dried by shaking or with fine blotting-paper (Royal). The preparation is then examined with a one-twelfth mm. oil-immersion lens. In order to obtain ideal results certain precautions must be heeded. All vessels with which the stain comes in contact must be perfectly clean. Before mixing each fresh lot of stain the test-tube used should be cleansed by scrubbing with clean cotton and alcohol, then rinsed with distilled water. Any deposit of stain about the neck and lip of the dropping-bottle should be removed by carefully wiping with filter-paper. The water used in making the glycerin solution and for washing the slide should be neutral, as the least degree of acidity causes the formation of a precipitate. Should any of these precautions be neglected, it will be found that a heavy bluish precipitate forms in the mixture on boiling and its staining ability is thus impaired. The exact tint of the smear to be obtained is a matter of no great importance and is easily determined. After a few trials, in which the importance of the above details is realized, one may expect to produce satisfactory preparations.

In preparations thus stained the Spirochæta pallida should appear a deep pink, with the background pale in comparison. It is a delicate, spiral-shaped organism, 4 to 14 μ in length and less than 0.25 μ in breadth. The ends are somewhat pointed. The convolutions number 6 to 14 or over. The Spirochæta refringens, frequently found in suggestive lesions, is to be distinguished by its greater width and by the relatively few convolutions.

Staining with *Goldhorn's solution*[3] is very simple and yields excellent results. The stain is dropped on the unfixed preparation and left for a few seconds. The

[1] For particulars about the fusiform bacilli and the spirochætæ that usually accompany them, as well as about the clinical picture of Vincent's angina, see Plaut, Deut. med. Woch., 1894, p. 922. Vincent, Ann. Past., 1896, p. 488, and 1899, p. 609. Reichs, Jahrb. d. Hamburgischen Staatskrankenhauses, 1903–04, vol. ix; also J. Douglas Blackwood, Proceedings of the Pathological Society of Philadelphia, 1906, No. 4, p. 103.

[2] White and Avery, The Treponema Pallidum, Arch. of Int. Med., June, 1909.

[3] Proc. New York Path. Soc., 1905, No. 5, p. 169.

slide is then slowly immersed in water, film side down, held so for four to five seconds to allow interaction between the water and the dye, and is then moved about in the water to wash it. It is then stood on end to drain and allowed to dry without the use of filter-paper or heat.

Hasting's stain may be used for smears made from the serum which exudes from syphilitic lesions. The technic is the same as for blood. (See p. 780.)

The so-called *India-ink method*[1] is perhaps the simplest and most satisfactory for demonstrating the organism. A loopful of serum, obtained from a syphilitic lesion in the manner described above, is mixed with a drop of the best obtainable commercial Chinese ink (Günther and Wagner's or Higgins' India ink) and spread out on the slide in the thinnest possible uniform layer, just as in making blood-smears. It is allowed to dry and can then be examined directly with an oil-immersion lens. The field is a homogeneous brownish yellow. Blood-cells and spirochætæ appear luminous white. Everything else is covered and hidden by the ink.

Should doubt arise concerning the specific nature of the organism found by the above methods of examination, the material should be examined in the fresh state, best by means of the dark-field illuminator (Reichert, Vienna). A drop of the serum is placed on a cover-slip and this is inverted on a slide 1 mm. thick. Both must be absolutely clean, and care must be taken to prevent the formation of bubbles. The spirochætæ, as well as other bacteria and the leukocytes, appear luminous on a black field.

Cultivation of Spirochæta Pallida.—Schereschewsky[2] has succeeded in securing a growth of the spirochæta at 37° C. in from three to five days on horse serum, which had been brought to gelatinous consistence and subjected to partial autolysis by standing about three days in a thermostat at 37° C. Inoculation of the growth so obtained into animals has not, however, proved successful.—Ed.]

Retropharyngeal abscesses present a visible and palpable swelling in the posterior pharyngeal wall. They may cause dyspnea. *Hypertrophied tonsils* are evident to inspection. *Adenoids* can be felt in the nasopharyngeal space. (See p. 869.) The mobility of the soft palate should also be noted. For a *paralysis of the palate* or for *absence of the palate reflex* (hysteria), see section upon Rhinoscopy and Laryngoscopy (pp. 897 and 904).

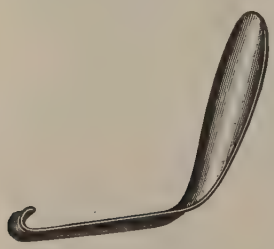


Fig. 329.—Lindt's palate hook for direct rhinoscopy.

Direct Rhinopharyngoscopy.—W. Lindt,[3] of Bern, has recently described a method for direct inspection of the nasopharyngeal space. This is accomplished by pulling the soft palate forward and upward by means of the palate hook depicted in Fig. 329.[4] With the illumination from an ordinary head-mirror, the posterior, lateral, and upper wall of the nasopharynx can thus be examined, and most easily if the head be bent slightly backward. The anterior and posterior walls of the soft palate must be cocainized (2 to 4 per cent. solution) in sensitive individuals. (See p. 899.) This method of examination is valuable especially for the purpose of detecting adenoids.

Hard Palate.—We should look especially for syphilitic perforation of the palate [for mucous and mycotic patches.—Ed.], and in children for the so-called Bednar's aphthæ.

Buccal Mucous Membrane.—Besides the conditions of the mu-

[1] R. Frühwald, Ueber den Nachweiss der Spirochæta pallida mittels des Tusche Verfahrens, Münch. med. Woch., Dec., 1909, p. 2523.

[2] Deutsch. med. Woch., July 22, 1909.

[3] Die directe Besichtigung und Behandlung der Gegend der Tonsilla pharyngea und der Plica salpingopharyngea in ihrem obersten Theile, Arch. f. Laryngologie, vol. vi, p. I.

[4] Made by Klöpfer in Bern.

cous membrane described in connection with other portions of the mouth, we may look for cancrum oris, stomatitis, etc. A rare gangrenous condition of the mucous membrane of the cheek called *noma* is sometimes found in children. Koplik's spots, an early sign in measles, should also be remembered. (See Plate XI.)

Secretion of Saliva.—Increased salivation accompanies all types of stomatitis and chronic mercury-poisoning. (In one of the author's cases this persisted for six months after a single dose of calomel.) The secretion of saliva is diminished in *fever, diabetes mellitus, cholera, atropin-poisoning*, and in *facial* and *bulbar paralysis*.

Examination of Saliva for Mercury for the Prevention of Mercurial Stomatitis During Treatment with Mercury.—Severino [1] says that the mouth secretions during administration of mercury give, on addition of tincture of iodin, a red color, due to the formation of mercury biniodid only in case the organism is oversaturated with the metal. In such an event it seems advisable to interrupt the use of mercury in order to prevent symptoms of poisoning with the drug, and especially the appearance of a stomatitis. Severino has devised a simple method of carrying out this test. He paints the anterior surface of the incisor teeth with tincture of iodin and then asks the patient to wet the teeth thoroughly with saliva. In case the reaction is positive, a more or less intense rose-colored stain appears on these teeth within half a minute.

EXAMINATION OF THE ESOPHAGUS

In the diagnosis of diseases of the esophagus we should be on the watch for disturbances in function, for pain upon swallowing, signs of stenosis or regurgitation, in addition to the direct method of examination about to be described. We must differentiate between regurgitated material from the esophagus and vomitus (p. 431). The surgical rules for palpation apply to the external examination of the cervical portion of the esophagus. One should look out for tumors which compress the esophagus, for swollen glands, for goiters, for sensitiveness along the course of the esophagus, etc. Diverticula of the esophagus are characterized by their variations in volume and by the fact that they can be emptied.

Esophageal Sounds or Tubes.—The well-known whalebone sounds, to the tip of which an ivory olive of varying caliber may be screwed or the English elastic tubes of varying caliber are employed. Before introducing one of these instruments we should be sure that they are in perfect condition, as a faulty instrument may sometimes injure the patient.

For certain purposes we make use of specially constructed sounds, such as those devised for the examination of diverticula. These sounds are so designed that it is possible to curve them in any direction after introducing them into the esophagus; in one case the physician is enabled to direct the sound into a diverticulum in order to examine it thoroughly; in another, in which ordinary sounds would enter the sac, he can slip past, either for the purpose of diagnosis or for feeding the patient through the sound.

Fig. 330 shows a longitudinal section of the tip of Zenker and Leube's diverticulum sound, that has been used for a long time for this purpose. The essential portion of this sound consists of a peculiarly constructed obturator, which contains

[1] La Sem. méd., 1906, p. 186, No. 16.

two parallel wires gliding through wire rings. The figure shows how the movement of these wires curves the jointed end of the obturator, and with it the tip of the sound. This obturator is introduced inside the lumen of an ordinary stomach-tube. One wire ends in a ring outside of the stomach-tube, and the other has a

Fig. 330.—Longitudinal section of the tip of Zenker and Leube's diverticulum sound.

Fig. 331.—The tip of the obturator in author's diverticulum sound.

cross-piece attached to its end, so that the operator can give any desired curve to the tip of the sound by manipulating the wires by means of these attachments. The author has constructed a very simple diverticulum sound designed upon a different principle. The essential part of this instrument, too, consists of a peculiarly constructed obturator, which is also used with a common stomach-tube. (See Fig. 331.) The obturator is made just like an olive-pointed bougie, from a piece of whalebone that is stiff and yet flexible. At its tip is attached a slim and rather flexible nickel-plated spring, terminating in an eccentrically placed cone made of German silver. The obturator is introduced into a rather thin stomach-tube with lateral fenestrations, which must be provided with a hollow blind tip beyond the fenestrations, so that the metal cone of the obturator may be fitted tightly into it. If the tube have no such tip, it may be made by burning out the solid tip with red-hot wire. The concavity of the spring and the projection of the metal cone should be directed to the side toward which the tube is to be bent; and the direction of the curve in the spring is marked upon the handle of the obturator.

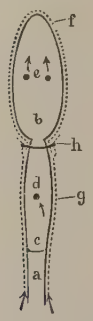


Fig. 332.—The author's dilatation sound.

If the operator push the obturator forward while holding back the stomach-tube, the latter must bend at the portion corresponding to the steel spring of the obturator and curve in any desired direction and to any desired degree. In addition to its simplicity the author's instrument possesses still another advantage, for when bent, it assumes a gradual curve and not a sharp angular one; moreover, its tip always retains a certain elasticity and softness. The author suggests the application of this principle in the construction of urethral catheters, such as those used in prostatic hypertrophy.

The author's dilating sound was designed for therapeutic purposes, more especially for gentle dilatation of the esophagus in spasm at the cardia, the most frequent

cause of spindle dilatations of the esophagus. However, it may be used for diagnostic purposes, as, for instance, to prove the dilatability of such spastic stenoses or for examining tuberculous bronchial glands. (See p. 896.) The instrument consists of a whalebone sound with a peculiar tip. (See Fig. 332.) Instead of the usual ivory olive, the author substitutes a German-silver one, *b*, which is provided with a canal that opens upon the surface of the olive by means of two perforations, *e*, and by means of a third, *d*, upon the surface of a metal link connecting the olive and the staff. For use, the metal olive is unscrewed, the whalebone staff is passed through a rather narrow stomach-tube, *g*, provided with a terminal central opening, and its tip allowed to project a little. The olive is then screwed on, covered with a rubber nipple, *f* (medicine-dropper); and the end of the stomach-tube is firmly tied over its free border. In the figure the rubber parts of the complete instrument are depicted by dotted lines, while the curved line, *h*, represents the ligature just described. The handle of the staff is likewise made removable, so as not to interfere with the following manipulations: Air blown into the interior of the rubber tube by means of a bulb is forced into the perforation, *d*, and then escapes through the perforations, *e*, into the rubber nipple, expanding the latter to any desired degree. The rubber tube, being provided with much thicker walls, is hardly affected by the air. The apparatus is connected with the air-bulb by means of a piece of glass tubing over which the end of the rubber tube is slipped, while the end of the whalebone staff, minus its handle, projects into the lumen of the glass tube. If the latter be provided with a lateral arm, a mercury manometer may be interpolated, so that, during the operation, the pressure exerted at the site of the obstruction may be estimated. If considerable pressure must be used, the olive may be covered with two rubber nipples. A single nipple is easily overdistended, balloons out into a large bag when in this condition, may burst suddenly, and the pressure it exercises upon the stenosed part is quite indeterminable. The author considers this dilating sound much to be preferred to those described in the literature, which are often difficult to obtain.

The technic of introducing these relatively stiff sounds differs somewhat from that employed in the use of soft stomach-tubes. (See p. 440.) The following is the best mode of procedure.

The esophageal bougie is held in the right hand, close to the end, very much like a pen; the tip is smeared with oil or glycerin, and the patient, in the sitting posture, is told to open his mouth and bend his head well back. The tip of the bougie, covered by two fingers of the left hand, is introduced into the pharynx, and pressed slightly forward. It is kept as nearly as possible in the median line. This position of the head has the advantage of placing the esophagus in the direction of the axis of the mouth, but if the introduction of the sound prove impossible, in spite of it the head of the patient should be inclined slightly forward. When the head is thrown backward, the cricoid cartilage is pressed backward too, and may interfere with the passage of the tip of the sound into the esophagus. However, individual patients differ in this respect, and the best thing to do is to control the head of the patient with the left hand during the introduction of the sound and bend it according to the resistance met with. It is most important that the sound should not deviate from the median line while being introduced; otherwise it may easily be caught in one of the pyriform sinuses. After overcoming the slight physiologic resistance at the level of the cricoid cartilage, the bougie will pass as far as the stomach with ease, provided there is no pathologic obstruction. Efforts to swallow are best avoided, as they are unnecessary and only induce gagging, on account of the contact of the soft palate with the bougie. It is important for the patient to breathe regularly. (See Stomach Examination, p. 441.) If the examiner be awkward, or if there be a paralysis or lack of sensation in the pharyngeal region, a hard bougie will enter the larynx more readily than a soft one. But this fault can be avoided easily if the point of the bougie, while

being introduced, be allowed to pass along the posterior wall of the pharynx. When hard hollow sounds are employed, a peculiar whistling respiratory noise arises on introduction (p. 441). An inexperienced operator may be alarmed by this, believing that the tube has entered the larynx. The noise is in reality produced by the respiratory variations of pressure in the interior of the thorax, which are transmitted in sufficient strength to the esophagus to produce an in-and-out current of air through the sound, unless its opening be occluded by the esophageal wall (esophageal breathing). This can be easily demonstrated by placing a burning candle before the end of a stomach-tube in position. The flame will flicker regularly with respiration. The greater size of the hard tubes and their resonance probably explain why this sound is much more intense when these are employed than when soft ones are introduced. The moment the tip of the sound enters the stomach, this noise ceases. If the sound enter the larynx, dyspnea almost always follows, and, unless the larynx be anesthetized, violent attacks of coughing and severe pain.

Kraus claims, however, that in less sensitive individuals the sound may be introduced into the larynx without causing any reaction. This is to be kept in mind especially in cases of paralysis of the gullet. In case of doubt it is easy to make sure that the sound is in the right place by palpation, using the epiglottis as a landmark. It must be said, however, that the introduction of an esophageal sound into the larynx is a very difficult feat, and the fear of such an accident is, for the most part, only theoretic. The existence of Zenker's diverticula forms an exception, the entrance to the esophagus being obstructed even at the level of the larynx. Introducing a sound into the larynx, in addition to causing injury to the parts, may be still more dangerous if fluids are poured through the tube, either for feeding the patient or for special diagnostic purposes (see below). However, this is generally done only after the operator has made sure of the position of the sound.

Esophageal sounds will demonstrate the presence of stenoses by transmitting a sensation of resistance to their advance. The most frequent cause of stenosis of the esophagus is carcinoma; then come diverticula, foreign bodies (bits of bone, false teeth, coins, etc.), syphilitic strictures, strictures from burns, compression of the esophagus from without by goiters, tumors, or aneurysms of the aorta, etc.

With signs of stenosis of the esophagus it is a good plan to attempt a working diagnosis regarding the nature of the disturbance before passing the sound, taking the history and the general condition into consideration. If aneurysm of the aorta be suspected, the sound should not be passed.

The sound, particularly by indicating the location of the obstruction, may throw some light on the nature of the stenosis. The following data should be remembered:

Distance from the incisor teeth to the uvula = 7 cm. ($2\frac{3}{4}$ in.).

Distance from the incisor teeth to the beginning of the esophagus = 15 cm. (6 in.).

Distance from the incisor teeth to the tracheal bifurcation = 23 to 25 cm. (9 to 10 in.).

Distance from the incisor teeth to the cardiac orifice = 40 cm. (16 in.).

The beginning of the esophagus lies at the level of the cricoid cartilage or of the sixth cervical vertebra, with the head midway between flexion and extension.

[The tracheal bifurcation (crossing of esophagus and the left bronchus) lies at the level of the fourth or fifth dorsal vertebra. The cardiac orifice lies opposite the spine of the twelfth dorsal vertebra or at the origin of the twelfth rib.—Ed.]

Length of the esophagus = 25 cm. (10 in.).

Length of its abdominal portion = 2 cm. ($\frac{3}{4}$ in.).

Other landmarks in the topographic anatomy of the neck may be mentioned here. The spinous process of the second cervical vertebra lies 2 cm. below the external occipital protuberance. It is, however, not always to be felt. The dorsum of the tongue is at the level of the middle of the second cervical vertebra.

With the help of these figures it is easy to determine approximately the site of the obstruction, by measuring the length of the sound introduced until resistance is encountered. It is to be remembered, however, that they are but the average measurements for normal adults, and vary somewhat according to the stature of individual patients. It is, therefore, always advisable to study the site of an obstruction still further by placing the sound externally along the patient's neck, holding it in the same position as it may be supposed to have assumed within the esophagus, and again noting the level reached by the tip of the sound.

The consistence of an obstruction is also of considerable importance. It may be shown by the feeling or the noise produced by contact of the sound, especially if the whole bone sound be used against a hard foreign body, such as pieces of bone, coins, etc.

It is also important to determine the degree of stenosis. This is accomplished by trying a series of sounds of decreasing caliber until one is found sufficiently small to slip through the obstruction. In the patient's interest we should not employ any force while making this attempt.

It is also necessary, if possible, to estimate the length of the obstruction. This is very difficult to determine with the ordinary stomach-tube, but quite simple if the obstruction be permeable with the whalebone sound. For this purpose the latter is furnished with an "olive" (of ivory or bone) which can be screwed or fastened over one end of the sound. Varying sizes of "olives" are necessary, so that one can be selected which will pass through the obstruction. After slipping by the obstruction the sound is withdrawn until the lower edge of the obstruction can be plainly felt; then, by comparing the position of the upper and the lower edge of the obstruction, we can readily determine its vertical extent. In the same way multiple obstructions can be located and measured.

Repeated examinations of an esophageal stenosis sometimes reveal this peculiarity—at one attempt the obstruction can be overcome very readily, while at another it is very difficult or quite impossible. Perhaps this depends upon the fact that the esophagus may alter its condition quickly, due to the destruction of ulceration or to the presence of food residue. Frequently, however, it depends upon some dilatation of the esophagus above the stenosis, so that the sound slips into a sort of pocket, and perhaps does not always meet the obstruction in exactly the same way. It may also be due to spasm of the esophagus, which may be added to the anatomic obstruction by the irritation in sounding. It is also possible that a saccular "pressure diverticulum" crowds against the esophagus, and when filled, compresses its lumen,

and so stops the sound, although, when the diverticulum is empty, the sound readily slips by. However, before assuming the existence of such a diverticulum, we should always bear in mind that the saccular "pressure diverticula" are found almost exclusively in the neck at the uppermost part of the esophagus, and if filled, are usually palpable externally; the so-called deep-seated pressure diverticula are very rare. Traction diverticula, which occur more frequently in the lower part of the esophagus, cause no stenosis.

In sounding the esophagus the exhibition of a localized tenderness at the moment when the tip of the sound passes over a definite place is of considerable diagnostic importance. Such a painful condition is observed in *carcinoma of the esophagus* and of the *cardiac orifice of the stomach*, even when there is no stenosis, in *inflammatory changes of the esophagus, esophagitis*, and in the rare circular *ulceration of the esophagus and of the cardiac orifice.*

With every attempt to sound the esophagus we should always carefully examine the sound as soon as it is withdrawn, and especially the fenestra at the tip of the stomach-tube if the latter be employed, in order to determine whether any fragments have been scraped off. Small bits of tissue not infrequently adhere in cases of carcinoma of the esophagus, and are often large enough to be sectioned after hardening in formalin, or with the aid of the freezing microtome. (See p. 516, note.) In this way the diagnosis of carcinoma may sometimes be confirmed. In "thrush" involving the esophagus, the fungus elements may be demonstrated microscopically in particles adhering to the withdrawn sound. (See p. 723, Fig. 291.) The fenestra of the sound frequently contain bloody mucus in carcinomatous and non-carcinomatous ulcerations of the esophagus. (For special findings in cases of carcinoma, diffuse dilatation, and diverticula of the esophagus, see p. 893.)

AUSCULTATION OF THE ESOPHAGUS

Other methods of examining the esophagus are subordinate to the methods of palpation and of sounding. *Auscultation of the esophagus* has thus far furnished rather barren results. Hamburger and Zenker auscultate the swallowing murmur in the neck upon the left side of the trachea, and in the chest to the left of the spine, at the level of the eighth dorsal vertebra. Here, during the act of swallowing, we can hear a peculiar clucking and hissing murmur. With pronounced esophageal stenoses the swallowing murmur may either disappear entirely or may be delayed from the level of the stenosis downward. Rewidzoff[1] has recently shown that the murmurs of swallowing described by Hamburger may be used in still another fashion in the diagnosis of esophageal stenosis. He auscultated the esophagus of patients suffering from stenosis at the level of the obstruction, first having them swallow a little water and then repeat the act of swallowing with an empty mouth; five to fifteen seconds after such acts of swallowing a hissing murmur could again be heard, some of the swallowed water having been retained above the obstruction in the first act, and passed through the obstruction by the subsequent acts of swallowing. Rewidzoff has termed these sounds *residual murmurs*, and speaks of the first, second, third residual murmur, etc. Meltzer[2] studied more minutely the murmur which arises upon the entrance of nourishment into the stomach, and which we hear best by auscultating the cardia with the stethoscope in the angle between the xiphoid process and the left costal margin. He arrived at the following conclusions: In normal individuals, six to seven seconds after the beginning of a single act of swallowing fluid or gruel, we hear at that point a more or less distinct prolonged murmur, as if the air or fluid were being squeezed through a sphincter-like obstruction (squeezing murmur). According to Kronecker and Meltzer's examinations, fluids are

[1] Rewidzoff, Berlin. klin. Woch., 1908, No. 15.
[2] Centralbl. f. d. med. Wissenschaften, 1883, No. 1.

squirted into the lowest part of the esophagus at the very commencement of the act of swallowing. Hence we are entitled to conclude from the delay of the murmur at the cardia that, normally, what is swallowed in each act of swallowing remains six to seven seconds just above the cardiac orifice before it reaches the stomach. With a relaxed (insufficient) or paralyzed cardiac orifice, a distinct murmur can be heard over the site of the cardia, immediately after the beginning of the act of swallowing (squirting murmur). If this "squirting murmur" be plainly heard, the later "squeezing murmur" is lacking. In this sense, the "squirting murmur" has been called first, and the "squeezing murmur" second. This terminology, however, may lead to the erroneous conception that these two murmurs necessarily belong together, that is, that they may be heard simultaneously in one and the same patient. The above discussion shows, on the contrary, that, in general, this is not true. The former shows that the action of the mylohyoid muscle and the base

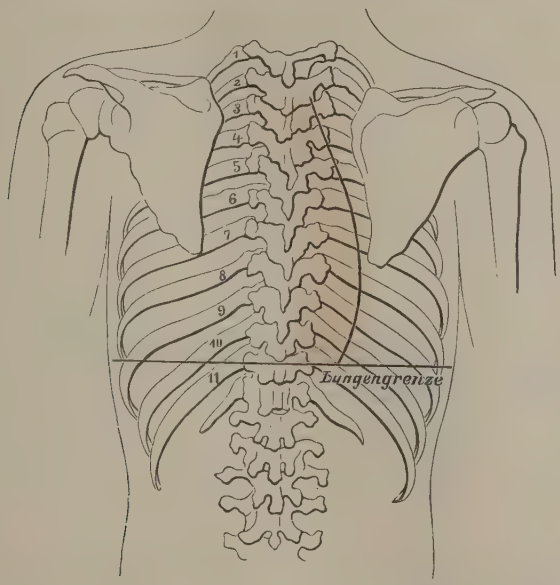


Fig. 333.—Spindle-shaped dilatation of the esophagus. Right-sided dulness shortly after swallowing considerable liquid, disappearing completely on regurgitation of the fluid. Diminished vesicular breathing over the dull area. An interesting feature of this case consisted in the dislocation of the heart to the left, as shown by percussion, each time the esophagus was filled; the organ resumed its former position, somewhat too far to the left, when the esophagus was emptied. Anteriorly, nothing else abnormal could be brought out by percussing. The figure shows that spindle-shaped dilatations of the esophagus develop principally to the right side of the vertebral column. (See Corning, Topographische Anatomie, 1907, Fig. 212, p. 279.)

of the tongue squirts the swallowed material directly into the stomach without any obstruction, the "squeezing murmur" being absent because the cardia is not closed as it should be in normal individuals. In the latter case, that is, in the presence of a normal obstruction at the cardia, the "squirting murmur" is absent. Meltzer states, however, that in exceptional cases both murmurs may follow each other and be indistinctly heard. Either one or the other murmur can be heard in all but very few cases. Swallowing warm fluids seems to make the "squeezing murmur" more distinct. It occurs earlier in weak individuals—perhaps three to four seconds after the act of swallowing. If several swallows succeed each other rapidly, the time relation varies. Either the "squirting murmurs" become more distinct with swallowing, even where each successive act of swallowing was not heard with a single act, or we hear only a "squeezing murmur" six to seven seconds after the last act of swallowing, or, finally, we may hear nothing at all. Meltzer considers the occurrence of a distinct "squirting murmur" after a single act of

swallowing as a trustworthy sign of insufficiency of the cardiac orifice. He found it in individuals who complained of regurgitating their food with coughing, and conspicuously in patients with advanced recurring syphilis. Meltzer's swallowing murmur has thus far proved of limited clinical value. Quincke[1] pointed to a decided objection in that the swallowing murmur is differently affected by the way in which the fluid is mixed with air during the swallowing, and by the condition of fulness of the stomach. However, the occurrence of a "squirting murmur" after a single act of swallowing may, in certain cases, be considered to signify an abnormal insufficiency of the cardiac orifice; absence of "squeezing murmurs," on the other hand, may signify stenosis of this orifice.

PERCUSSION OF THE ESOPHAGUS

Percussion of the esophagus may, in rare instances, aid in the diagnosis of large "pressure diverticula" of the esophagus. If the diverticulum be filled with air, a tympanitic note can be elicited in the cervical region or at the superior thoracic aperture. If the diverticulum contain food or liquid, the note will be dulled or flat. The variations depending upon the ingestion of nourishment are especially characteristic and important for the diagnosis.

Characteristic percussion phenomena may likewise be occasionally obtained over a diffuse dilatation of the esophagus if it be distended with food. In a case observed by the author dulness was present on the right side, along the whole extent of the dorsal vertebræ. (See accompanying figure.)

ESOPHAGOSCOPY

Esophagoscopy is the inspection of the esophagus with the aid of a specially constructed instrument, a so-called esophagoscope, furnished with electric illumina-

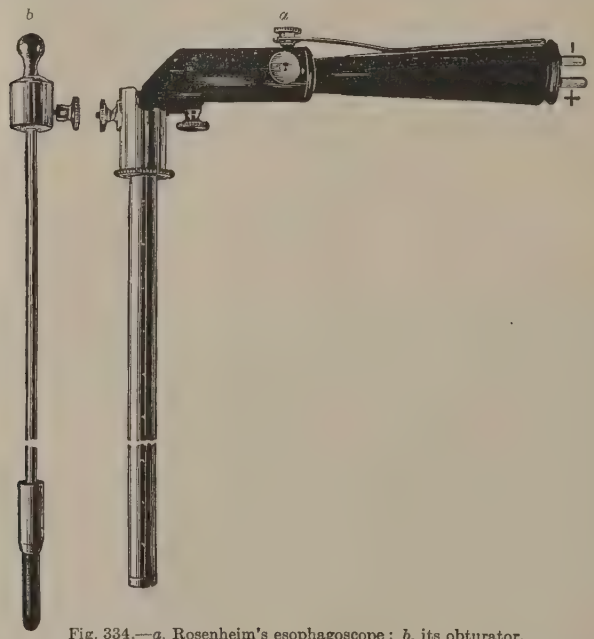


Fig. 334.—*a*, Rosenheim's esophagoscope; *b*, its obturator.

tion. This method has recently been so perfected by the introduction of more suitable instruments that it can be carried out without any special danger or dis-

[1] Arch. f. exper. Path., vol. xxii, p. 395

comfort to the patient. Esophagoscopy has been developed through the labors of Störck, Kussmaul, Mikulicz, Kelling, von Hacker, Killian, Starck, Rosenheim, Brünings, and others; at the present time Rosenheim's and Brüning's instruments are the most used. Rosenheim's instrument, which is analogous in principle to other endoscopic apparatus, is pictured in Fig. 334. It consists essentially of a perfectly straight tube with a circular opening at its lower end; a handle attached at right angles to its long axis; and an obturator (Fig. 334, *b*) which is removed after the introduction of the tube. The complete apparatus is furnished with several interchangeable tubes of different length and diameter, the latter measurements varying from 11.5 to 13 mm., with sponge-holders for wiping the interior of the tube, forceps for extracting foreign bodies, and sounds. Casper's panelectroscope attached to the handle (Fig. 334, *a*) supplies the light. It consists of a small incandescent lamp whose light is directed into the tube in parallel rays by means of a plane mirror. This attachment has the disadvantage of obstructing one-half of the lumen of the tube, as is plainly seen in the accompanying illustration; introduction of instruments for cleansing the field of vision or for operative purposes is thus difficult. Accordingly, Starck recommends Kirstein's electric head-lamp as a more suitable source of light; one hand of the operator controls the esophagoscope, while the other is employed in manipulating the instruments introduced through the tube. Earlier operators made use of laryngeal reflectors, which were attached to the forehead of the examiner, while still others made use of a small electric lamp attached to the lower opening of the tube, as in Strauss's rectoscope (Fig. 211, p. 503). The laryngeal mirror, however, does not furnish a sufficient amount of illumination, while the introduction of an electric lamp into the tube obstructs too much space within its lumen. Before introducing the instrument, the pharynx, especially the lateral pharyngeal walls, the region of the cricoid cartilage and of the pyriform sinuses should be anesthetized with a 10 per cent. solution of cocain. Starck recommends a 3 per cent. solution of β-eucain. In less sensitive patients who have been repeatedly examined it is possible to introduce the esophagoscope without preliminary cocainization. Rosenheim recommends the patient to lie on his back upon the examination table, with his head hanging down directly backward; but von Hacker introduces the instrument with the patient in the sitting posture on the middle of the operating table, with bared throat and thorax, and places him on his back after introduction. The physician stands on a stool to the right of the patient; behind the latter stands an assistant ready to support and move the patient's head. The operator presses the back of the tongue as far forward as possible with his left index-finger; with his right hand he introduces the instrument, previously lubricated with vaselin, and with its obturator in place, into the entrance of the esophagus, following the right pharyngeal wall and pushing aside the right corner of the mouth. During this manœuver the patient holds his head as erect as possible; but then his head is slowly bent backward while the instrument is pushed onward. After the instrument has been introduced, the patient is slowly lowered to a horizontal position, with his head hanging down backward off the operating table. The obturator is then removed, the illuminating apparatus is brought into action, and the whole esophagus examined, the tube being carefully moved up and down. Kraus also introduces the esophagoscope in the sitting posture, unless the patient be troubled with excessive secretion of mucus; he, however, places the patient upon a low footstool. If, however, there be difficulty in wiping away the mucus, he makes use of von Hacker's method, afterward bringing the patient in the horizontal position, with his head hanging over the edge of the table. This procedure allows the mucus to escape out of the mouth by itself.

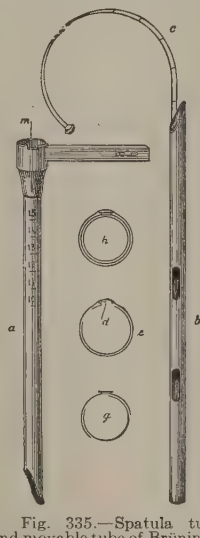


Fig. 335.—Spatula tube and movable tube of Brünings' esophagobronchoscope.

Recently esophagoscopy has been further perfected and simplified, as far as illumination is concerned, by the introduction of *Brünings' esophagobronchoscope* (Figs. 335 and 336.) With his instrument both bronchoscopy and direct laryngoscopy may also be carried out. (See Autoscopy or Orthoscopy of the Larynx, p. 901.) The essential modification consists in the substitution of two telescoping tubes for

the one tube of the esophagoscope, one of them being called the spatula tube and the second the movable tube (Fig. 335, *a* and *b*). The latter tube fits accurately into the former and can be pushed forward in its lumen by means of a weighted watch-spring *c*. This arrangement greatly simplifies the necessary manipulations, because it allows one to lengthen the esophagoscope after the introduction of the instrument; in addition, the tube does not stick out from the patient's mouth in such an inconvenient manner as is the case with the older instrument, when the upper portions of the esophagus are examined. The *spatula* is provided with a centimeter scale which is measured from the end of the tube, though the markings begin at a distance of 10 cm. from that end (Fig. 335). A similar scale, seen in the

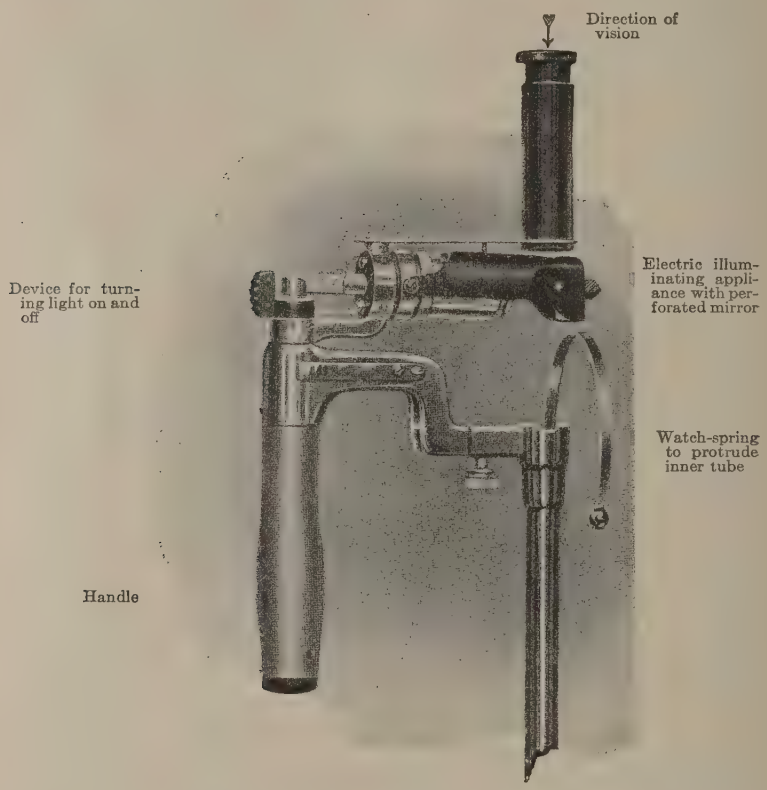


Fig. 336.—Brünings' bronchoesophagoscope.

picture, is marked upon the watch-spring attached to the inner tube of the instrument. These scales enable the observer to estimate the depth to which the inner tube is introduced, as well as the total length of the tube at any stage of the examination. The introduction of the *spatula* is facilitated by employing an obturator constructed out of the flexible material used in bougies; it is made pointed at one end and projects beyond the end of the tube. A further modification, useful if the obturator be not used, consists in the slightly curved, bill-like lower end of the tube designed to overcome the angle between the mouth and the esophagus (Fig. 335). Brünings' instrument is provided with a perfected illuminating apparatus (Fig. 336), light being derived from a small electric lamp the rays of which are made parallel

by passing through a lens. This light falls on a plane mirror which makes an angle of 45 degrees with the long axis of the tube, thus throwing the light into the interior parallel to this axis: the observer looks directly into the lumen of the tube through a central opening in the mirror, as in the ophthalmoscope. This illuminating apparatus, which is firmly attached to the tube of the esophagoscope, can be rotated to one side, thus making the tube more accessible. The incandescent lamp is provided with a specially constructed filament, the light being concentrated upon a single point upon which the movable illuminating lens can be exactly focused. This arrangement results in very intense illumination. Brünings' apparatus is, in addition, provided with various accessory parts, such as a pump for removing the saliva, sponge-holders, forceps for foreign bodies, etc. For bronchoscopy the makers supply smaller tubes, which can be attached to the handle containing the illuminating apparatus (Valentin's salpingoscopy, etc.). The instrument is sold by M. Schärer in Bern.

The rules given for esophagoscopy in general apply to the use of Brünings' instrument. For details the book of instructions accompanying the instrument may be consulted, as well as Brünings' work, entitled Die Technik der Bronchoscopie und Oesophagoskopie, Bergmann, Wiesbaden, 1908. Starck's monograph (Würzburg, A. Stuber's Verlag, 1905) may also be consulted, for it contains a historic review of the development of this method of examination.

So far as the pictures obtained by the esophagoscope are concerned, the following data will suffice here. The cervical portion of the esophagus appears through the instrument as a closed tube, because of the pressure of surrounding parts; its thoracic portion, on the other hand, appears wide open, because of the negative pressure within the thorax, so that the observer is able to see a considerable portion of the organ beyond the end of the esophagoscopic tube. The color of the normal esophageal mucous membrane is pale red. Esophagoscopy allows one to observe pathologic changes very easily, such as catarrhal and ulcerative processes, peptic ulcer of the esophagus, ulcers caused by foreign bodies, scars due to syphilitic lesions and to burns by caustics, carcinomata, etc. The latter may be observed in their early stages, while examination with sounds demonstrates them only when far advanced. A purely spastic esophageal stenosis can be demonstrated perfectly by this method, the esophagoscopic picture in such a case showing no anatomic changes in the walls of the esophagus whatever. In cases of diffuse dilatation of the esophagus the observer finds that the view into the lower portions of the organ, which normally is wide open, is obstructed by folds of mucous membrane encroaching upon the lumen, but which are easily pushed aside. The mouth of Zenker's pharyngo-esophageal pressure diverticulum is difficult to see by this method, because it is found at the very entrance of the esophagus, and is, therefore, hidden by the instrument as soon as it is introduced to the depth of a few centimeters. For special findings the reader is referred to the consideration of the various affections of the esophagus.

MEASUREMENT OF PRESSURE IN THE ESOPHAGUS

Mikulicz [1] has furnished interesting and important information in reference to the measurement of the intraesophageal pressure, which indicates both the motor power of the esophageal musculature and the tonus of the cardia. It is necessary to have a mercury manometer with an index of 100 mm.; the pocket mercury manometer described upon p. 165 may be employed. A thin, soft-rubber esophageal tube (see p. 439), of sufficient resistance to overcome lateral compression, is introduced into the esophagus until its open end is at the level of the manubrium. Before the introduction of the tube its outer end is clamped, and the clamp is not removed until the tube has been connected with the manometer. When the clamp is removed, the mercury usually falls, indicating that the end of the tube is within the thoracic portion of the esophagus. When the patient swallows, the mercury rises, and this elevation, according to Mikulicz, should amount to about 10 mm. A diminution of this pressure may be due either to atony of the esophageal musculature or to a diminished tonus of the cardia, which latter, by relaxing, would prevent the production of a greater pressure. The tonus of the cardia is now estimated by determining the pressure at which fluids flow into the stomach. For this purpose a T-tube is inserted between the esophageal tube and the manometer, and its horizontal limb connected with a funnel by rubber tubing. Fluid at body temperature is then poured into the funnel, and the pressure is read from the manometer at the

[1] Deut. med. Woch., 1904, Nos. 1 and 2.

moment the fluid commences to run into the stomach. In carrying out the latter manipulation the lower end of the esophageal tube must be pushed down to just above the cardia, otherwise the hydrostatic pressure of the column of fluid collecting between the opening in the end of the tube and the cardia would be lost. Since the tube and its connections with the manometer are filled with fluid, care must also be taken to bring the zero-point of the manometer to the level of the cardia, since it is at this point that we wish to determine the pressure. According to Mikulicz the initial pressure at which lukewarm, indifferent fluids flow into the stomach varies between 2 and 17 mm. of mercury. The resistance of the cardia is shown by the values obtained by this method. Abnormally low or high pressures are indicative of corresponding variations in the tonus of the cardia. With due regard to the results obtained by this method, we may determine whether a low or a high pressure during deglutition is due simply to a diminished or an increased resistance of the cardia or to abnormal conditions of the esophageal musculature. After the introduction of the fluid, it is well for the patient to repeat the act of deglutition, when the pressure should be measured again.

This procedure may also be employed for the estimation of the capacity of the esophagus, which is of importance for the diagnosis of diffuse esophageal dilatation, a subject about which so much has recently been written. The greater the amount of fluid which can be poured into the esophagus before any of it escapes into the stomach, the greater is the esophageal capacity. If such a diffuse esophageal dilatation be due to cardiospasm, as is usually the case, it will be found not only that a large quantity of fluid may be introduced into the esophagus before any of it flows into the stomach, as indicated by a sudden fall of the mercury, but that the fluid does not enter the stomach until it is acted upon by an abnormally high pressure.

THE PERMEABILITY OF THE CARDIAC ORIFICE OF THE STOMACH FROM THE STOMACH TOWARD THE ESOPHAGUS

For practical purposes it is usual to determine the permeability of the cardiac orifice in the direction from the esophagus toward the stomach. Meltzer, however, has pointed out the importance of determining the permeability of this orifice in the opposite direction, from the stomach toward the esophagus. He first questions the patient as to his ability or inability to vomit or to retch. Tickling of the pharynx without producing vomiting can sometimes be demonstrated. This he determines if the answers to his questions suggest its advisability. Further data are obtained by attempting to fill the stomach with air through a stomach-tube. Normally, the air escapes back through the tube after a moderate degree of distention has been reached; but in cases of spastic stenosis of the cardiac orifice the air remains in the stomach, to the discomfort of the patient, though a high degree of pressure has been reached. On the other hand, in insufficiency of this orifice or in carcinoma at the cardia interfering with its closure, it is quite impossible to distend the stomach to any noticeable extent, for the air introduced through the tube escapes almost immediately. These observations, if critically applied, are valuable in the determination of functional disturbances, such as form the foundation for abnormal eructation and vomiting, as well as for that curious regurgitation phenomenon termed merycism or rumination. In his study of the mechanism of eructation Meltzer has found that in this act, just as in vomiting, the cardiac orifice is opened with the help of the abdominal muscles and the diaphragm, escape of air occurring when this has taken place; after each act of eructation the esophagus contracts in a peristaltic wave, from above downward, without the assistance of the constrictors of the pharynx. Meltzer has found further that there may occur eructation of air from the esophagus proper and not from the stomach; this is differentiated from eructations originating in the stomach by the absence of a murmur on auscultating the epigastric region.

RÖNTGENOLOGIC EXAMINATION OF THE ESOPHAGUS

Both fluoroscopic examination and *x*-ray photographs of the esophagus may be used in diagnosis. The heart shadow interferes with the recognition of the esophagus if the latter be viewed in the sagittal direction; it is, therefore, advisable to direct the rays from the left side toward the back and from the right side toward the front. This position hides the heart shadow almost completely, both on the screen and in photographs, because of the great distance of the heart from the screen or the plate; but the esophagus becomes as plainly visible as if the heart had been completely removed. If the patient swallow some bismuth mixture, made

by thoroughly mixing 10 to 20 gm. of bismuth subnitrate or, better, the less toxic bismuth carbonate with potato porridge, the portion of the esophagus which contains this substance appears as a shadow in the fluoroscope or on the radiograph. If stenosis exist, the lower end or the narrowed portion of the bismuth shadow closely corresponds to it, and any dilatation above the obstruction may also be directly visible. Diverticula and diffuse dilatations of the esophagus exhibit an especially clear picture in this method of examination. Still another device, more suitable for fluoroscopy than for *x*-ray photography, consists in the introduction of a semi-flexible tube to the tip of which is tied an empty rubber balloon; this balloon is wound up spirally about the sound before the introduction of the latter, and is well lubricated. The balloon is then gradually inflated by means of a rubber bulb attached to the external end of the tube, and appears as a bright space in the fluoroscopic picture. By varying the degree of inflation of the balloon and by moving it up and down it is possible, so to speak, optically to palpate the esophagus. This procedure is especially suitable for the recognition of diffuse dilatations. To facilitate the recognition of the topography of the esophagus the blind end of the balloon may be filled with a dessertspoonful of bismuth subnitrate before attaching it to the tube; in such a case it appears as a dark shadow in the fluoroscopic picture below the bright space which represents the rest of the balloon. The same result may be obtained by filling the balloon, after its introduction, with a watery suspension of bismuth. The choice of methods depends upon the character of the "*x*-ray" tubes used, now one, now the other, giving the best results. It is also possible, of course, to combine both principles of examination, that is, the production of the light space and of the shadow, by first filling the balloon with air and then with bismuth suspension. In diffuse dilatations useful observations may be obtained occasionally by fluoroscopy after introducing a tube filled with shot or quicksilver. If, as is usually the case in this condition, an obstruction be present at the cardia, and if a marked diffuse dilatation of the esophagus have resulted, the tube is to be seen curved upon itself in the dilated portion, the size and shape of the curve allowing judgment upon the caliber of the dilatation. A semisolid sound provided with a wire obturator may be used for this purpose.

SPECIAL FINDINGS IN THE MOST IMPORTANT AFFECTIONS OF THE ESOPHAGUS

Carcinomata of the Esophagus.—The most important procedure in the diagnosis of carcinoma of the esophagus is examination with the sound, by means of which an obstruction is usually discovered if thick, olive-pointed bougies be used, and the diameter of the stenosed portion be determined by passing sounds of various calibers. If the obstructed portion be permeable, its vertical extent is determined by finding the difference between the position of the obstruction in passing the sound and in withdrawing it. In the great majority of cases esophageal carcinomata are found at the level of the tracheal bifurcation, that is, at a distance of 23 to 25 cm. [9 to 10 in.—Ed.] from the incisor teeth. The obstruction due to the presence of carcinomata may be found to vary in degree on different examinations, as a result of the varying spastic conditions induced in the esophagus and the different degrees of destruction in the morbid tissue. If the nature of the obstruction be in doubt, a clue may be obtained by examining with hard or moderately soft tubes possessing lateral fenestrations (p. 445 et seq.); on withdrawing the tube, particles of cancer tissue are frequently found in the fenestrations. As a rule, esophagoscopy immediately reveals the carcinomatous nature of the obstruction. This is the only method which allows an early diagnosis of this condition by the demonstration of a characteristic cancerous growth, for occasionally, in the early stages of the disease, no obstruction is perceived on passing sounds, though difficulty in swallowing may be present. An early diagnosis may yet become of more practical importance if the negative or the positive pneumatic pressure methods render them more accessible to operation. On the other hand, if the cancerous growth be still covered by intact mucous membrane, the tumor may not be apparent on esophagoscopic examination, because above it the tube of the instrument may be obstructed by the swelling due to submucous infiltration of the tissue. The act of swallowing in patients suffering from esophageal carcinoma is characteristic of the affection. Just as in all true stenoses of the esophagus, this act is performed very carefully after thorough mastication, because the patients have learned that swallowing is possible only when such care is exercised, while hasty swallowing usually leads to an immediate regurgitation of the food. The diagnostic significance of metastases in the regional lymph-nodes, in the lungs,

and the mediastinum, as well as the significance of certain paralytic phenomena, such as the paralysis of the recurrent laryngeal nerve or of the papillary fibers of the sympathetic, together with the study of perforations of cancer in the neighboring structures, will be considered in the sections on Special Diagnosis.

Diverticula of the Esophagus.—As is well known, only the saccular pressure diverticula are of clinical importance, so far as difficulty in swallowing is concerned. Two varieties of these diverticula are recognized—the high-seated diverticula, taking their origin at the level of the cricoid cartilage, and the deep-seated pressure diverticula, found in the midthoracic portion of the esophagus. The first-named structures are also called Zenker's or esophagopharyngeal diverticula, and probably depend for their origin upon congenital defects of the musculature of the esophagus and pharynx. The peculiar findings obtained in passing sounds into the esophagus form the principal factors in the demonstration of saccular diverticula. On one occasion, the obstruction which is caused simply by the pressure exercised upon the gullet by the filled sac may be overcome in passing the sound, and the latter may reach the stomach; on another, this proves to be impossible, different results being obtained with different degree, of distention of the sacs. If the passage of the sound prove possible, either an elastic obstruction, which is easily overcome, is encountered or no obstruction at all is felt, depending upon the condition of the sac at the time. Of course, if the sound enter the sac, the obstruction proves to be impermeable. These variable findings may lead to the suspicion that a diverticulum exists, but a positive diagnosis cannot be made from them alone because, as we have seen, obstruction due to carcinoma may lead to similar conditions. Differential diagnosis between these two conditions is made from the results of examination by means of a diverticulum sound (see p. 882), which usually shows that the tip of the sound passes the obstruction or is arrested, according to the direction given to it. Pharyngo-esophageal or Zenker's diverticula are usually directed backward from the esophagus; the deep-seated diverticula, originating on the level of the tracheal bifurcation, on the other hand, are situated in front of the gullet. The diverticulum sound must, therefore, be directed according to these usual situations of the diverticula; in order to overcome the obstruction in the former the tip must be directed forward, and in the latter backward. The fact that large quantities of decomposing food may be obtained if the sound enter the diverticulum is another characteristic of this condition. (See p. 431 for the differences between gastric contents and the contents of diverticula.) The act of swallowing is performed just as deliberately as with carcinoma, because swallowing, is often possible when done in this manner; whereas, if rapid, the sac is filled and makes further descent of food impossible. Patients suffering from high-seated Zenker's diverticula often help themselves out in a very characteristic manner by compressing the mass which, in swallowing, forms upon one side of the throat. Often they make various peculiar movements of the head in order to assist swallowing. In the presence of a diverticulum, regurgitation is usually much more abundant and occurs later than in carcinoma; in the latter regurgitation often follows almost immediately upon the act of swallowing, because no marked dilatation is present above the obstruction. A visible and palpable prominence on one side of the neck, forming immediately after the act of swallowing, is characteristic of a high-seated Zenker's diverticulum; this swelling is tympanitic when filled with air, and gives a dull note on percussion when filled with fluid or solid material. Occasionally the diverticulum is large enough to reach into the thorax; and then these variations in percussion may then be observed in the upper portions of the thorax, usually anteriorly, because Zenker's diverticula, although originating from the posterior surface of the esophagus, increase and spread forward in accommodating themselves to the free space in the thorax. The dull note over these diverticula usually disappears and is replaced by a tympany after the patient has vomited the fluid contents of the sac. Deep-seated diverticula furnish similar dull areas to percussion, which are to be looked for on the posterior surface of the thorax, in the neighborhood of the spinal column.

Diffuse (Spindle-shaped) Dilatation of the Esophagus.—This affection is rare, but important, from the standpoint of diagnosis, being usually dependent upon a spastic condition of the cardiac orifice. The first sign it manifests is the existence of an elastic obstruction (cardiospasm) at the level of the cardia, which is readily overcome if the examiner employ a fairly soft tube and exercise a little patience. It is very characteristic of this affection that before the obstruction is overcome a longer portion of the sound can be pushed down than would correspond to the position of the cardia that is, more than 40 cm. [16 in.—Ed.] as measured from the incisor teeth. This can evidently be accounted for by the deviation of the soft tube toward one side of the dilated esophagus. If the force with which the

sound is pushed downward be diminished before the obstruction is overcome the sound appears to spring back a few centimeters. After the sound has penetrated the cardiac orifice, the sensation of an elastic constriction about it is communicated to the hand, although after this is overcome, the sound can be pushed on further with only a certain amount of difficulty. Large quantities of food-remains are frequently obtained through the tube when it enters the esophagus. These remains may be recognized as coming from the esophagus by their alkaline or at most faintly acid reaction, or at least by the failure to give a reaction for free hydrochloric acid with Congo red. (See p. 449.) If the tube have passed the cardia and the stomach still contain food ingested not too long before the examination, gastric contents may be expressed, which can be easily recognized by the positive reaction for free hydrochloric acid with Congo red. If, however, the stomach be found empty or the material obtained do not contain free hydrochloric acid, the last-mentioned evidence of the fact that the cardiac obstruction has been overcome cannot be obtained. After a certain experience, however, the other signs cited above are quite sufficient to decide whether the tube is still in the esophagus or in the stomach. In addition, other tests may be mentioned. If liquid be introduced and the tube withdrawn, the patient can generally discriminate between the sensation of discomfort and oppression which accompanies overdistention of the esophagus from that of a filled stomach. The patient cannot voluntarily regurgitate the fluid introduced into the stomach, although he usually can the contents of a dilated esophagus and with ease. In cases of a diffuse dilatation of the esophagus it is possible to bend the tip of a diverticulum sound strongly at any level without meeting any well-marked resistance and without causing the patient any pain. As contrasted with the condition in the common strictures of the esophagus the type of swallowing in patients suffering from diffuse dilatation of the esophagus is quite characteristic. They usually swallow very rapidly and in large gulps. They hastily pour down large quantities of fluid, because the marked increase of pressure thus produced in the esophagus carries down at least a portion of the swallowed material into the stomach. The patient practically uses the last portions swallowed as a piston to push down the lower strata of the food into the stomach. Röntgenologic examination plays an important rôle in and has materially simplified the diagnosis of these diffuse dilatations. The technical devices used in this method of diagnosis, such as the use of a sound filled with mercury or with lead, the introduction into the esophagus of a balloon, which is then inflated with air or filled with a suspension of bismuth, the introduction of a bismuth mixture into the dilated esophagus itself, etc., have been described on p. 892. All these methods furnish good results, the best of them being those obtained by photographing the esophagus after the introduction of the bismuth mixture from the right side toward the front or from the left side toward the back, with the plate in front of and the tube behind the patient. The measurement of the intraesophageal pressure (see p. 891) may sometimes be used in the diagnosis. (For the views of the diffuse dilatations of the esophagus obtained by the esophagoscope see p. 891.) Auscultation of the thoracic portions of the esophagus (Hamburger's swallowing murmurs, see p. 881) gives almost normal results in the presence of a diffuse dilatation. In the majority of cases the affection is due to the presence of a cardiospasm, and, therefore, in the auscultation of the epigastrium the squirting murmur of Kronecker and Meltzer, as well as the squeezing murmur, are often either entirely absent or very indistinct; frequently they are very much delayed. (See p. 882.) In one case of a diffuse dilatation of the esophagus the author obtained very characteristic percussion findings. When the patient filled his esophagus by drinking water or by swallowing food, there appeared a characteristic zone of diminished resonance, narrower in its upper portions, along the right side of the spinal column. Evidently this zone of diminished resonance was caused by the overfilled esophagus compressing the neighboring part of the lung; the auscultation phenomena in the lung were not in any way characteristic, but the apex of the heart was displaced toward the left, even when the esophagus was empty, probably because of the continued pressure upon it. As soon as the patient regurgitated the material that filled his esophagus, the zone of dulness in the chest disappeared and the heart was less displaced. The author does not know whether similar observations have been made in any other case.

Mention must also be made of Rumpel's experiment for differentiating spindle-shaped dilatations of the esophagus from deep-seated diverticula. Rumpel introduces an elastic tube which, in addition to the end opening, has a number of lateral perforations in its lower half. When it is certain that the tip of this tube is in the stomach, a second and smaller tube is introduced into the esophagus alongside of the first one until a resistance is encountered. Water is then poured into the esoph-

agus through the latter. If a spindle-shaped dilatation be present, the water immediately flows into the stomach through the lateral perforations in the tube first introduced, so that none of it may be recovered through a second tube. If there be a diverticulum, however, at least a portion of the water introduced may sometimes be siphoned out through the second tube. A number of difficulties are encountered in carrying out this experiment. In the first place, it is not always easy to introduce the first tube or to determine that it extends into the stomach, since it may become bent upon itself either in a spindle-shaped dilatation or in a diverticulum. If a diverticulum be present, moreover, it is not such a simple matter to introduce the second tube into it The first difficulty may be overcome by performing the experiment upon a full stomach, and introducing the first tube so far that all the perforations are presumably in the stomach; the gastric contents are then siphoned out, indicating that the tube has really passed the cardia. The tube is then withdrawn until only the open end remains in the stomach, and the experiment is then carried out in the usual manner. To diagnose a diverticulum, it is necessary not only to introduce a tube into it, but also to recover through this tube a part or all of the fluid introduced. A diverticulum sound may be substituted in order to reach the diverticulum more readily.

In view of these difficulties, and the further one of introducing a second tube alongside of one already in the esophagus, the author adds a procedure suggested by Richartz [1] for the differentiation of spindle-shaped dilatations of the esophagus from deep-placed esophageal diverticula. The dilated esophagus is well irrigated, so that all particles of food are removed. A tube similar to that used by Rumpel, with an end opening and numerous lateral perforations, is then introduced almost to the cardia. This tube is connected with a funnel. The esophagus is then thoroughly irrigated with a solution of methylene-blue, the fluid being introduced and withdrawn a number of times, so as to be sure that a diverticulum, if present, is filled with the methylene-blue solution. If the patient strain slightly, some of the solution will be forced back into the funnel, proving that the tip of the tube is within the esophagus. The tube is now slowly pushed down into the cardia, allowed to remain there a short time, and then drawn back to its former position. In pushing the tube downward, the fluid in the esophagus runs into the stomach. Clear water is then introduced into the esophagus through the funnel and recovered by siphonage, and this procedure is repeated several times. If a fusiform dilatation be present, the water returns colorless; whereas if there be a diverticulum, the returning water will be intensely stained from the retained methylene-blue solution.

Under certain circumstances, Rumpel's experiment may be simplified by introducing the perforated tube just to the cardia, filling the esophagus with water, and then pushing the tube downward into the stomach, when the water will flow into the stomach, provided that it has not been caught by a diverticulum. The tube is then withdrawn until the end is just above the cardia. If the patient, by straining slightly, is now able to empty a portion of the fluid introduced, it necessarily follows that a diverticulum must be present.

These and similar experiments may be carried out with variations dependent upon the individual case.

The introduction of *x*-rays has, however, made these procedures quite superfluous; indeed, Röntgenologic examination has taken their place almost completely, because of the discomfort caused by them to the patient and the frequently uncertain results furnished by their use.

APPENDIX.—THE DEMONSTRATION OF ENLARGED TRACHEAL AND BRONCHIAL LYMPH-NODES

Enlarged tracheal or bronchial lymph-nodes cannot, as a rule, be demonstrated by percussion, and even Röntgenologic examination shows them only when they are greatly hypertrophied. E. Neisser[2] has, therefore, proposed to test the sensitiveness to pressure of such tuberculous glands by means of a sound introduced into the esophagus and then distended. The nodes that come within the possible field of this examination are, in Sukienrikow's terminology,[3] the inferior and the left tracheobronchial lymph-nodes, that is, the group situated in the obtuse angle formed by the trachea and the left bronchus, and those found between the two main bronchi. These two groups are immediately adjacent to the esophagus, while

[1] Deut. med. Woch., 1904, No. 21.
[2] Neisser, Deut. Arch. f. klin. Med., 1905, vol. lxxxvi, p. 28.
[3] Berlin. klin. Woch., 1903, vol. xvi.

the right tracheobronchial group of glands, as well as the bronchopulmonary group situated in the hilum of the lung itself, cannnot be approached from the esophagus. E. Neisser's procedure in testing the sensitiveness of these nodes consists in the introduction of a soft narrow sound to the tip of which a finger-cot has been tied. By means of a Politzer bag connected with the external end of the sound tube the finger-cot is then inflated at the level of the bifurcation. In examining different levels by this means it is advisable to allow the finger-cot to collapse before changing the position of the tube, and then reinflate it at another level. The author believes that the same results may be obtained by using Trousseau's olive-pointed sounds of appropriate caliber. The dilatation sound described on p. 882 (Fig. 332) may, however, be selected to carry out Neisser's procedure; the only change necessary is to arm the tip of the sound with a thin instead of the usual thick finger-cot. With this modification the amount of pressure employed can be estimated more easily, and, in addition, none is lost in transmission, because of the less resistance of the thin-walled covering.

LARYNGOSCOPY AND TRACHEOSCOPY; AUTOSCOPY OF THE LARYNX AND TRACHEA; BRONCHOSCOPY

EXAMINATION WITH THE AID OF A MIRROR

Since the invention of the laryngeal mirror by Garcia, Türk, and Czermak, mirror examination has played the most important part in the diagnosis of diseases of the larynx and trachea.

The principle of this method of examination is as follows: A reflector (a perforated, slightly concave mirror), which is ordinarily fastened to the examiner's head so that the central opening is opposite one of his eyes, collects the rays of light from the source of illumination (Argand burner, Welsbach light, electric light, or student lamp) and converges them into the back of the patient's throat upon a small mirror attached to a handle at an angle of about 45 degrees. The reflector and the laryngeal mirror are so arranged as to throw an intense illumination into the larynx, and at the same time reflect a virtual image of the illuminated parts to the examiner's eye.

In the ordinary position the base of the tongue hides the opening of the larynx, so that it is necessary for the patient to protrude his tongue as far as possible, while the examiner at the same time holds it firmly in position with a napkin or towel. Fig. 337 and the following pages explain the methods of application of the laryngoscope. Fig. 338 shows the path of the rays of light in laryngoscopy and tracheoscopy. The latter figure clearly illustrates the fact that to see the larynx plainly the laryngeal mirror must be held more vertically and introduced further backward; whereas, to observe the trachea, it must be held more horizontally and farther forward. The lower the handle is depressed, the more the parts which lie still farther backward come into the field of vision. The following sequence in the appearance of the parts in the field of vision is accomplished by gradually depressing the handle of the mirror: epiglottis and base of the tongue, anterior commissure of the vocal cords and anterior laryngeal wall, anterior tracheal wall, bifurcation, posterior tracheal wall, posterior laryngeal wall, and arytenoid cartilages. Fig. 339, copied from Heitzmann, represents a normal laryngeal picture.

A Few Details for the Practical Employment of Laryngoscopy.—The source of light and the heads of the examiner and patient should be practically at the same level. The laryngeal mirror should be heated over the lamp immediately before each introduction, to prevent its being diminished by condensed moisture.[1] In warming the mirror the glass slide should be held at some distance above the flame, and the degree of warmth tested by touching the back of the mirror to the examiner's hand. Not only is it necessary for the examiner to hold the tongue firmly as well as carefully, but it should be actively protruded by the patient, as otherwise a little pain and a reflex bulging of the posterior part may be produced, and thus render the examination difficult. To prevent gagging the examiner should carefully avoid touching

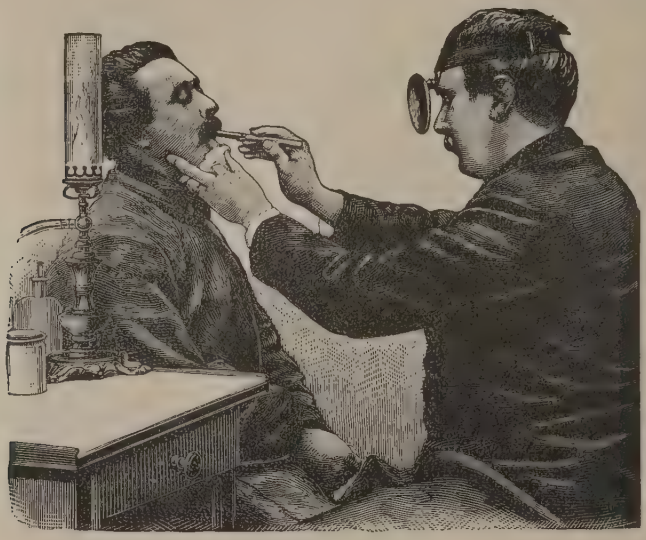


Fig. 337.—Technic of laryngoscopy.

with the mirror the pharynx, and especially the posterior pharyngeal wall and the base of the tongue. Touching the uvula ordinarily causes less trouble, and, as it so often drops down in front of the mirror, one can sometimes simplify the examination by supporting and pressing it upward and backward with the back of the mirror. The examination is almost always facilitated by convincing the patient that it is not in any way painful, and that, even though at the beginning the procedure may produce gagging, quiet and patience will always accomplish the result. The patient should always inhale quietly and regularly, and should say "Ah" with expiration, thus elevating the epiglottis, and so permit the examination of the interior of the larynx. If the epiglottis be depressed enough to obstruct the view, saying "ee" will usually elevate it sufficiently. It is rarely necessary to employ an

[1] The same purpose can be accomplished by coating the surface of the mirror with a very thin invisible layer of soap [or with a solution of lysol.—Ed.].

instrument which has been constructed for the purpose of elevating the epiglottis, nor to cocainize the pharynx, provided one takes the time and has the patience to get the patient somewhat accustomed to the examination. If cocain is to be employed, the pharynx should be painted with 5 per cent. solution of cocain hydrochlorid, and the patient should be instructed to spit out the solution immediately after its application, in order to prevent intoxication. In examining the larynx we should pay particular attention to the mobility of the parts, especially the vocal

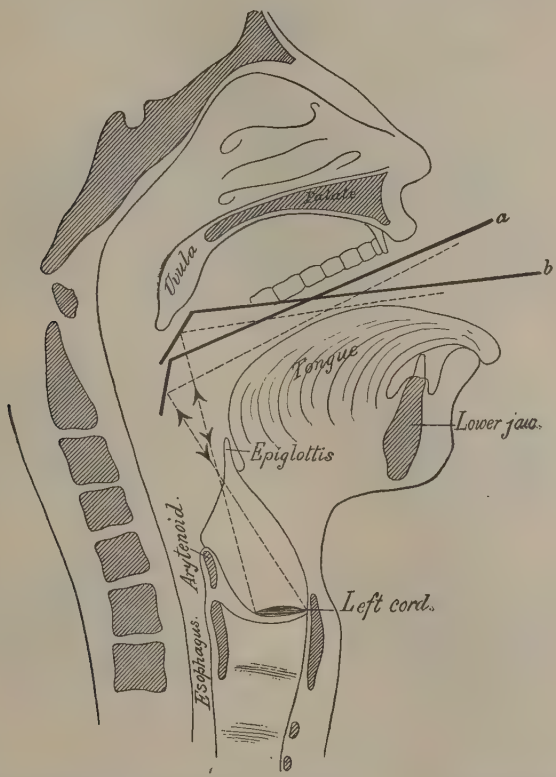


Fig. 338.—Diagrammatic representation of direction of rays of light in laryngoscopy and tracheoscopy (sagittal section of head and neck): *a*, Position of mirror for laryngoscopy; *b*, position of mirror for tracheoscopy.

cords, to their color, to accidental alterations in the surface (swelling, ulcerations, coating with mucus, etc.). It is impossible to go into a detailed description of the results of examination, and so the author will limit himself to appending the accompanying illustrations, which represent a few of the commonest and most important findings.

The same principles and rules apply to **tracheoscopy.** The patient should, however, sit considerably higher than the physician, so that the mirror can be held more horizontally and looked up into from below. Further, the patient should hold his trunk and neck quite

straight, and at the same time bend his head forward at the atlanto-occipital joint (chin against the neck). This position brings the axis of the pharynx into a more favorable position for tracheoscopy. The trachea cannot be observed well in all individuals, but in many we can get a view as far as the bifurcation without any special difficulty. In such cases all sorts of tracheal stenoses can be examined and recognized. Fig. 347 represents the normal tracheoscopic picture with the anterior

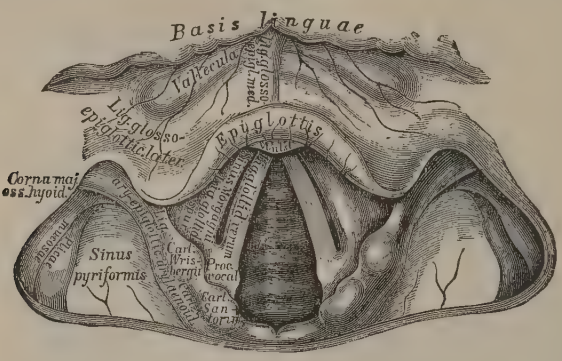


Fig. 339.—Normal laryngeal picture (after Heitzmann).

tracheal wall. Fig. 348 represents the same with the posterior tracheal wall (a different position of the mirror). Both show the bifurcation of the trachea.

Inferior tracheoscopy or *laryngoscopy* means the examination of the trachea or larynx from a tracheotomy wound. For this purpose we

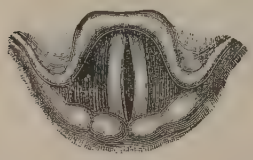


Fig. 340.—Paralysis of both thyro-arytenoidei int. (tensors), due to acute laryngitis. Position of cords during phonation (after von Ziemssen).

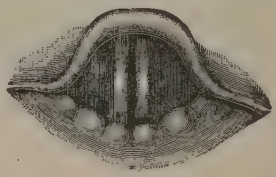


Fig. 341.—Posticus paralysis. Bilateral complete paralysis of crico-arytenoidei postici (dilators) at moment of inspiration (after von Ziemssen).

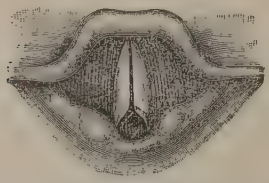


Fig. 342.—Arytenoideus paralysis. Paralysis of interarytenoidei transversi and oblicui (respiratory closers of glottis) in laryngitis. Position of cords in phonation with open glottis respiratoria (after von Ziemssen).

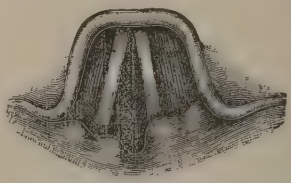


Fig. 343.—Recurrence paralysis. Cadaveric position of left cord (midway between adduction and abduction, with complete paralysis of laryngeus recurrens sin.). Inspiratory position of right cord (after von Ziemssen).

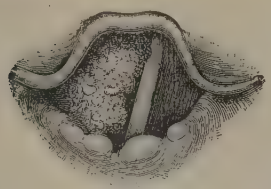


Fig. 344.—Carcinoma of the right false and true cords. Anterior commissure of cords pushed to left (after von Ziemssen).

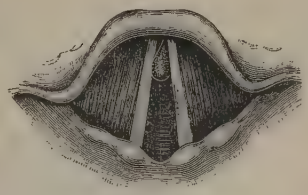


Fig. 345.—Pedunculated fibrous polyp arising from lower surface of left cord. Inspiratory position (after von Ziemssen).

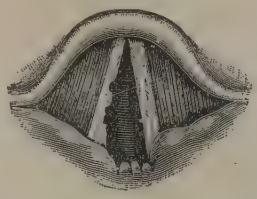


Fig. 346.—First stage of tuberculosis of larynx. Ulceration of right cord and swelling of interarytenoid region, with formation of folds. Possibly early ulceration here.

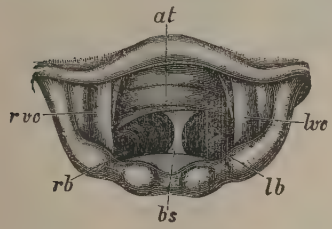


Fig. 347.—Tracheoscopic picture of anterior tracheal wall and of bifurcation: *at*, Anterior tracheal wall; *rvc* and *lvc*, right and left cords; *rb* and *lb*, right and left main bronchi; *bs*, seat of bifurcation (after Mackenzie).

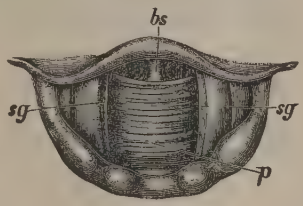


Fig. 348.—Tracheoscopic picture of posterior tracheal wall and bifurcation: *p*, Posterior tracheal wall; *sg*, regio subglottica; *bs*, seat of bifurcations (after Mackenzie).

employ a so-called "subglottic mirror," which is constructed in quite the same fashion as the laryngeal mirror, except that it is much smaller (diameter of 7 to 10 mm.). This is introduced through the tracheal wound, and the illumination is thrown in from the reflector in the same way as described above. Its principal use is to determine the causes which prevent the withdrawal of the cannula in croup operations.

DIRECT EXAMINATION OF THE LARYNX, TRACHEA, AND BRONCHI

(Autoscopy; Orthoscopy; Direct Laryngoscopy, and Tracheoscopy)

A. Kirstein[1] has described a method of examining the larynx and trachea without employing a mirror. The base of the tongue is drawn forward with the aid of a spatula-shaped instrument, and the larynx and trachea are then examined directly. Kirstein described this method under a rather unfortunate term—"autoscopy"

[1] Therap. Monatshefte, 1895, vol. ix, p. 361; ibid., 1896, p. 370; Encyklop. Jahrbücher, 1896, vol. vi, p. 30.

of the larynx and trachea. It would seem more correct to name the procedure "orthoscopy of the larynx and trachea," or "direct laryngoscopy and direct tracheoscopy" (as opposed to indirect or mirror laryngoscopy and tracheoscopy). Kirstein employs for direct laryngoscopy the instrument pictured in Fig. 349, the so-called "autoscope"; but for most cases he has more recently substituted a simpler instrument, which is nothing but a tongue depressor of a particular shape (Fig. 351). The original "autoscope" is now recommended by Kirstein only for performing autoscopic operations for demonstration and for examining children.

The "autoscope" (Fig. 349, 1) consists of a grooved metallic spatula (*S*), about 12 cm. long and about 3 cm. wide. The groove varies from 1 to 2.5 cm. in depth. It is removable and is attached at a right angle to the handle (*G*), and well rounded off to prevent injury. The anterior end (*d*) of the spatula is quite sharply bent downward; and attached to its end, next to the handle, is an electric lighting apparatus (not shown in the figure), so arranged that a cone of rays is transmitted by means of a prism along the groove exactly in its long axis. A contact contrivance for the electric light is shown in the figure. The part *r*, which is movable, forms a kind of a roof or sheath to the grooved spatula, and so prevents the upper lip or the mustache from obstructing the view. The application of the instrument can be readily understood by studying Fig. 350.

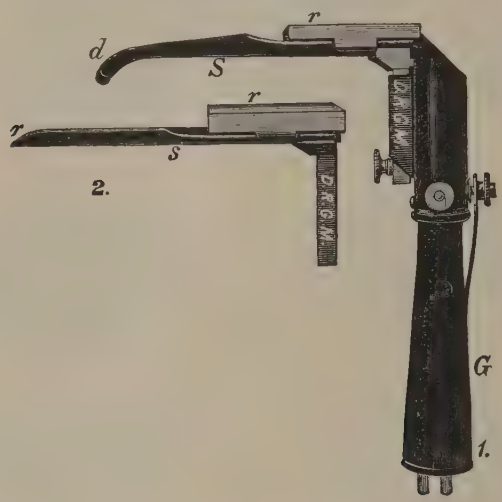


Fig. 349.—Kirstein's autoscope: 1, Ordinary spatula; 2, intralaryngeal spatula.

The instrument is grasped by the handle and inserted so that the tip of the grooved spatula lies between the base of the tongue and the epiglottis. The base of the tongue is then hooked downward and forward by raising the handle of the instrument a little, and the epiglottis is slightly raised by pulling upon the median glosso-epiglottic ligament. Pressure upon the teeth must be avoided. If the epiglottis obscure the view into the larynx, cocain may be applied and the instrument introduced directly behind the epiglottis. For this purpose a differently shaped spatula (Fig. 349, 2) is employed.

After the instrument is properly introduced, the examiner looks down between the upper teeth and the grooved spatula with the aid of the electric illuminator. Fig. 350 illustrates the position of the patient, with the trunk bent slightly forward and the head thrown back a little. This position brings the axis of the larynx and trachea in as direct a line as possible with the axis of the mouth. Brünings' esophagoscope (see p. 889 et seq.) is quite as, or even more, suitable for autoscopy than Kirstein's original instrument. The only thing necessary is to leave out the inner tube and use simply the spatula-shaped tube of the instrument. Experience has led Kirstein to recommend the instrument pictured in Fig. 351 (a simple tongue spatula with a special groove) for most cases where direct laryngoscopy is advisable. The

illumination is furnished by the ordinary head-mirror. The advantage of Kirstein's method is that the parts are seen more naturally than by a mirror, with richer and more vivid shades of color. Nevertheless, the author is convinced that direct laryngoscopy will never usurp the place of mirror laryngoscopy. The appli-

Fig. 350.—Technic of autoscopy (Kirstein).

cation of the instrument is much more disagreeable to most individuals than indirect laryngoscopy, and almost always necessitates the employment of cocain. Besides, we can rarely view the entire larynx, and still less the trachea. In many cases the anatomic position of the parts is such that we do not see any further than to the epiglottis. The method furnishes very incomplete conclusions about the

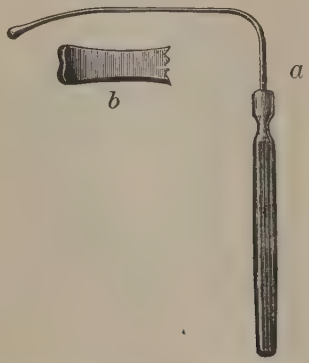


Fig. 351.—Kirstein's tongue spatula for autoscopy; *a*, Lateral view; *b*, end of spatula, seen from above.

motility of the larynx, because the mobility of the parts is disturbed by the examination. Advantages of the method, however, are the directness of the picture and the ease with which the posterior parts of the larynx can be examined. These are very difficult to see in the ordinary laryngeal mirror, and, if seen, are sharply foreshortened;

they are very important in the diagnosis of initial tuberculosis affecting the arytenoid folds. Still other advantages are that direct laryngoscopy can be usually accomplished quite easily in small children; that in difficult cases the examination can be effected under chloroform anesthesia; that it decidedly simplifies intralaryngeal operations, and that it allows of such operations to be carried on under anesthesia.

Kirstein has even succeeded in introducing a small, so-called subglottic mirror into the larynx of patients who have been cocainized. He attached this with a long rod to the autoscope, and was able to examine the inferior surface of the vocal cords.

It must be acknowledged that considerable practice is necessary for orthoscopy as well as for the mirror examinations. To any one who is accustomed to the indirect or mirror laryngoscopy, the direct picture is so unusual that it is quite difficult to orient properly the apparently transposed parts, and still more difficult to correct certain habits of movement in the application of instruments, etc.

BRONCHOSCOPY

The procedure of bronchoscopy has recently been so perfected that it is possible to inspect the interior of the bronchi by means of an endoscopic appliance, which may be introduced either through the intact larynx or through a tracheotomy wound. Although this procedure has already been proved to be of considerable value, particularly for the extraction of foreign bodies, it will not be described, since it is difficult of application by the general practitioner. The most suitable instrument for bronchoscopy is the one invented by Brünings, and used for esophagoscopy as well. (See p. 889.) The only change necessary is to use thin and short tubes in the instrument instead of the longer and thicker ones with which the esophagus is viewed.

COMBINED LARYNGOSCOPY

Kirstein and, later, Leo have recommended a combination of direct and indirect laryngoscopy, under the name of "combined laryngoscopy," for cases which are very difficult to examine. The base of the tongue is depressed with the spatula of the orthoscope, and then the laryngoscopic mirror is introduced much farther down into the depths of the throat opposite the epiglottis.

RHINOSCOPY

The nasal cavities can be examined from in front and from behind within the pharynx. In the former case we speak of *anterior rhinoscopy;* in the latter case, of *posterior rhinoscopy.*

For **anterior rhinoscopy** we employ a nasal speculum to dilate the nasal openings a little, and then illuminate the nasal cavities from

Fig. 352.—Fränkel's nasal speculum (one-half natural size).

in front by a light reflected from a head-mirror. In this way we can observe the nasal septum, the inferior and a part of the middle turbinate bone. Quite exceptionally we also can see a small part of the superior turbinate bone. A very serviceable nasal speculum is pictured in Fig. 352. Catarrhal conditions of the nasal mucous membranes are readily recognized by *anterior rhinoscopy;* also the dilatation of the nasal cavities

due to the atrophy of ozena, nasal polypi, and the peculiar vasomotor engorgement of the erectile tissues in nervous nasal affections and in hay-fever. The latter is especially pronounced in the inferior turbinate bone.

Posterior rhinoscopy depends upon the same principle as laryngoscopy. A cone of rays is thrown from the reflector upon a small laryngeal mirror, which is introduced behind the uvula, with its reflect-

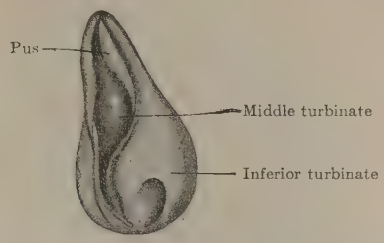


Fig. 353.—Anterior rhinoscopic picture in empyema of left frontal sinus. Characteristic collection of pus lateral to the middle turbinate bone and high up in the upper position of the middle nasal fossa (after a colored drawing by R. Krieg, Atlas of Diseases of the Nose, Stuttgart, Enke, 1900).

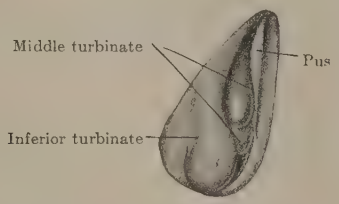


Fig. 354.—Anterior rhinoscopic picture in empyema of right sphenoid sinus. Collection of pus, the site of which is typical for an affection of the sinus and of certain ethmoid cells (after a colored drawing by R. Krieg, Atlas of Diseases of the Nose, Stuttgart, Enke, 1901).

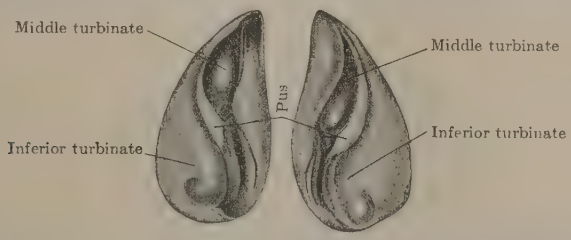


Fig. 355.—Anterior rhinoscopic picture in empyema of the antrum of Highmore. Bilateral collection of pus between the middle and the lower turbinate bones in the middle and lower portions of the middle nasal fossa. This site is characteristic for affections of this cavity and of certain sphenoid cells (after a colored drawing by R. Krieg, Atlas of Diseases of the Nose, Stuttgart, Enke, 1901).

ing surface turned upward and forward. This mirror reflects the illumination to the posterior nares and transmits the reflected image of these parts to the observer's eyes. The path of the rays of light and the position of the mirror are shown in Fig. 356. In regard to the practical application of *posterior rhinoscopy*, the following differences between it and laryngoscopy should be noted: The tongue should not be protruded; we use a very much smaller laryngeal mirror—perhaps

the smallest size; we must be very careful not to touch any part of the pharyngeal wall; and the mirror is introduced behind or below the

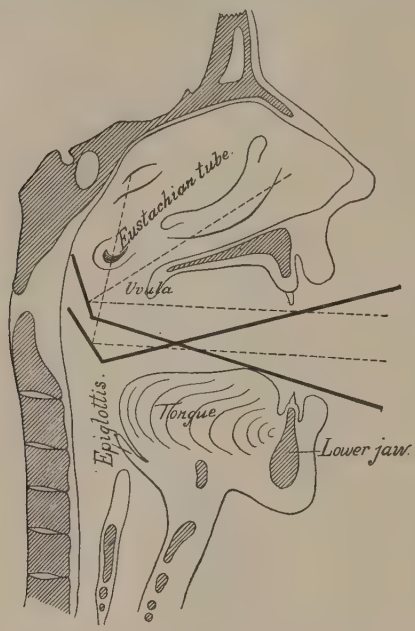


Fig. 356.—Course of light-rays in posterior rhinoscopy. Sagittal section of head.

soft palate, its reflecting surface being directed upward and forward. The patient simply breathes naturally with a relaxed palate and does

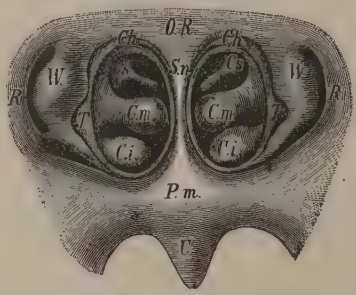


Fig. 357.—Normal picture in posterior rhinoscopy. Diagrammatic in that to obtain a complete picture the position of mirror must be repeatedly changed: *S.n.*, Septum; *Ch.*, choanæ; *P.m.*, soft palate; *U.*, uvula; *C.i.*, lower turbinate bone; *C.m.*, middle turbinate bone; *C.s.*, upper turbinate bone; beneath each turbinate the corresponding fossa; *O.R.*, roof of pharynx; *T.*, opening of Eustachian tube; *W.*, promontory of tube; *R.*, Rosenmüller's fossa (after Schnitzler).

not intone. If the root of the tongue bulge upward, it may be depressed by means of a tongue-depressor, held by the examiner's left hand, or sometimes by the shaft of the mirror. By accustoming the patient to

this method, it will succeed just as well as in laryngoscopy, even in very difficult cases. If success be impossible otherwise, cocain may be employed.

Fig. 357 represents a normal picture in *posterior rhinoscopy*. The main object of posterior rhinoscopy is to observe: adenoid vegetations and tumors of the nasopharynx, nasal polypi, inflammatory affections

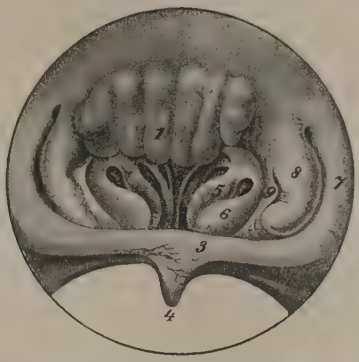


Fig. 358.—Posterior rhinoscopic picture in a case of adenoid vegetations (hyperplasia of the pharyngeal tonsil, slightly modified from a colored drawing of Brühl[1]): 1, Hyperplastic pharyngeal tonsil; 2, vomer; 3, soft palate; 4, uvula; 5, middle turbinate bone. Above it, superior turbinate bone; 6, inferior turbinate bone; 7, fossa of Rosenmüller; 8, promontory of the tube; 9, pharyngeal opening of the Eustachian tube.

of the nasal cavities, alterations in the openings of the Eustachian tubes in middle-ear disease, etc. (See p. 901 in regard to completing posterior rhinoscopy by direct rhinopharyngoscopy.)

OPHTHALMOSCOPY

Without going into the technic of ophthalmoscopy, a description of the more important changes in the eye-grounds will be given:

In Plates 9 and 11 several of these conditions are pictured. The drawings have been generally made in the upright image, though they have been reduced to the size of the inverted image.

Plate 9, *Figs.* 1, 2, and 3.—Various forms or stages of optic neuritis and choked disk.

Fig. 1. *Beginning Optic Neuritis.*—The disk is congested, the temporal margin is slightly veiled and swollen, the veins are moderately dilated and tortuous, the arteries are somewhat contracted.

Fig. 2. *Pronounced Optic Neuritis.*—The disk is apparently enlarged, with ill-defined margins. It presents radial striations, and is opaque from exudates and hemorrhages; it is very congested and swollen. The veins are greatly dilated; the arteries very much constricted.

Fig. 3. *Optic Neuritis of the Highest Grade—So-called Choked Disk.*—The disk is ill defined. It is prominent, like a mushroom, and projects 2 to 3 mm. There is a difference in refraction of at least two diopters between the apex of the swelling and the surrounding retina. The vessels make a sharp bend at the papillary margin. The disk at its margin is gray. In the center it is covered by a white exudate, which masks the congestion. The veins are very much dilated and tortuous; the arteries

[1] Brühl and Politzer, Atlas of Otology, Saunders, 1906.

stomum anemia, and in leukemia. The changes are not so intense and usually not so pronounced in the severe anemias of certain cancers of the stomach, and are practically absent in simple chlorosis.

Fig. 7. *The Eye-ground in Hereditary Syphilis.*—Perivasculitis of the retinal vessels and choroiditis. Perivasculitis is especially characteristic for syphilis. The vessels, especially the arteries, appear to be outlined in white, owing to thickening of their walls. In one place the changes are so pronounced that a vessel is converted into a white strand, through which the blood-current can no longer be observed. The picture presents the characteristic spots of choroidal atrophy, and pigment deposits in the choroid. The macula lutea is especially plainly visible.

Fig. 8. *Choroidal Tubercle in Acute Miliary Tuberculosis.*—The choroidal tubercles are characterized as ill-defined white spots, which become more intensely white with age, usually round, and measuring one-quarter to one-half a papilla in diameter. In the later stages they are larger, and their site is independent of the course of the blood-vessels. If they be situated in the region of a blood-vessel, they are covered by the latter. The drawing shows recent and old tubercles. Especially characteristic in cases where the nature of these structures is not clear is their sudden appearance and increase within a few days. They can be distinguished from retinal spots by their usually circular form and their ill-defined margins. In the case depicted in the figure, in addition to the miliary tubercles, there was a complicating tuberculous meningitis, which explains the hyperemic and blurred appearance of the disk (beginning neuritis). Contrary to a widespread belief, the presence of choroidal tubercles is a rarity in uncomplicated tuberculous meningitis. Choroidal tubercles in almost all cases point to the presence of a general miliary tuberculosis. The characteristic condition of a tuberculous meningitis is, on the other hand, optic neuritis or choked disk.

Fig. 9. *Medullated nerve-fibers of the retina,* presenting a white, glistening, flame-shaped figure, beginning at the disk and striated radially. In the upper part of the picture a retinal blood-vessel is partly covered by this white structure; otherwise, the eye-ground is normal. This condition is anomalous, but without functional ignificance. It must, however, be recognized in order to distinguish it from pathologic changes.

Plate 11 gives a summary of the ophthalmoscopic pictures occurring in the various forms of optic atrophy, which are of great diagnostic interest.

Fig. 1. *Simple Atrophy of the Optic Disk.*—The disk is white and shining, the margins are unusually sharp, the light scleral ring is visible, especially on the temporal side, the lamina cribrosa appears as a glistening network, including angular, grayish areas representing bundles of atrophic nerve-fibers. The excavation of the atrophic disk is shallow, like that of a plate, and therefore recognized with difficulty. The color of the disk is usually most pale about the entrance of the blood-vessels and in the temporal half of the disk. The caliber of the blood-vessels usually remains normal. The very small blood-vessels which furnish nutrition to the disk are usually very few and fine. The large vessels, especially the arteries, usually diminish in size only after the atrophy has existed for a long time. The atrophic excavation of the disk develops generally only in the later stages, beginning at the margin of the disk and gradually proceeding to the center.

To distinguish this simple atrophy from inflammatory atrophy it is of importance to note the normal condition of the blood-vessels, the visibility of the lamina cribrosa, the well-defined margins of the disk, with distinct scleral ring.

Simple atrophy occurs most frequently in tabes dorsalis and in progressive paralysis; furthermore, in the so-called primary gray degeneration of the optic nerve without spinal or cerebral symptoms. In some cases of multiple sclerosis simple optic atrophy has occurred; in others, neuritic atrophy. It should further be mentioned that simple atrophy of the optic nerve may occur if there be an interruption in the course of the optic nerve or of the optic tract, as in chronic hydrocephalus, where the distended infundibulum presses upon the chiasm.

Fig. 2. *Atrophy of the Optic Disk After Embolism of the Central Artery, Following Ligation of the Common Carotid in a Case of Pulsating Exophthalmos.*—Complete blindness. The disk is grayish-white. The margins have a distinct scleral ring; the lamina cribrosa is visible. In the center the central canal appears as a grayish dot. The vessels are contracted to mere threads.

Fig. 3. *Atrophy (Pressure Atrophy) of the Optic Nerve in Glaucoma Simplex.*—Complete blindness. The disk is grayish white; the lamina appears in the center. The entire disk is deeply excavated. The vessels make a sharp bend at the margin and disappear in the depth. A few again appear at the bottom of the excavation; some are broader and lighter in color because of differences in refraction. The

veins are somewhat dilated, the arteries slightly contracted. There is a yellow area with several pigment spots about the excavated disk (halo glaucomatosus).

Fig. 4. Neuritic Atrophy of the Optic Disk.—Incomplete blindness. The disk appears dull white; the nasal half is still slightly red in color. The margins of the disk are ill defined, without a distinct scleral ring. The lamina cribrosa is not visible. The vessels are moderately contracted, especially the arteries. Some are surrounded by narrow white lines characteristic for sclerosis of the vessel-wall. Occasionally pigment is present in the form of small spots at the margin of the disk. These features (ill-defined margins of the disk, contraction of the blood-vessels, invisibility of lamina cribrosa and scleral ring) differentiate this form from that of simple atrophy.

Any inflammation in the course of the optic nerve may lead to neuritic atrophy. In some of the cases of multiple sclerosis, as has been above stated, the atrophies observed have been of an inflammatory type. The illustration is of one of these cases.

Fig. 5. Papillitic Atrophy.—Blindness. The disk is dull white and uniformly discolored. The margins are even less sharp than in Fig. 4, passing over into the choroidal changes which surround the disk (the pigment is often lacking; in other cases it is deposited irregularly). The lamina cribrosa is invisible. The vessels are distinctly contracted. These changes represent simply a higher grade of neuritic atrophy (Fig. 4), which is spoken of as papillitic atrophy, because in its occurrence the disk is included in the neuritic process. Consequently papillitic atrophy is a frequent sequence to true choked disk, especially in brain tumors. As the choked disk proceeds to atrophy, the disk remains swollen for some time, the vessels show a distinct bend, as in Fig. 3, Pl. XII, while it gradually assumes more and more the character of papillitic atrophy (whitish discoloration, narrowing of the blood-vessels). In this condition the color of the disk is often a dirty grayish yellow.

Fig. 6. Papillitic Atrophy after Thrombosis of the Central Retinal Vein, Following Chronic Meningitis.—The disk is discolored, grayish white. Its margin on one side is distorted. It is surrounded and partly obscured by extensive changes in the choroid and pigment accumulations. In the center the central canal appears as a grayish dot. The vessels are converted into thin white strands (progressive organized thrombosis). In this form the condition of the blood-vessels is characteristic.

Fig. 7. Retinal Atrophy in Old Chorioretinitis.—The latter affection in this case was the result of unusually prolonged lactation, and presumably developed upon a syphilitic basis. In any case, it resembled certain late stages of syphilitic chorioretinitis. Incomplete blindness. The disk is of a uniformly dirty-yellowish-gray color. The margins in this case are sharply defined; sometimes, however, they are blurred. The lamina markings are not visible. The vessels are unusually narrow. The retina and the choroid are very much changed, the choroidal vessels presenting evidences of sclerosis. The intravascular spaces are dark. There is moderate pigment accumulation in the retina.

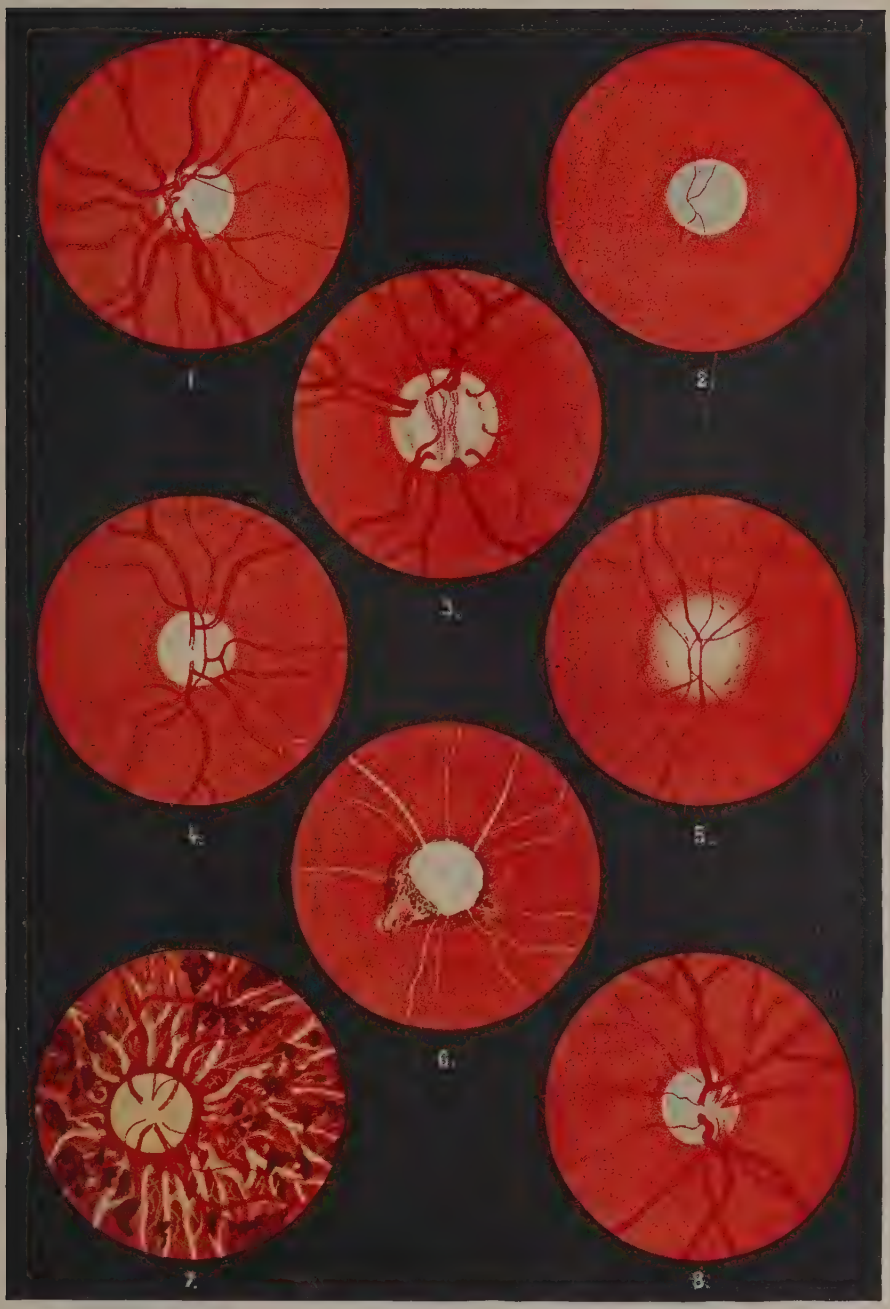
Similar changes of the disk to those which have just been described may occur in retinitis pigmentosa and in other chronic inflammatory processes of the retina, as well as in detachment of the retina. The retinal and choroidal changes are characteristic in differential diagnosis from other optic atrophies.

Fig. 8. Atrophic Discoloration of the Temporal Half of the Disk in Alcohol Amblyopia (Central Scotoma for Green and Red; Vision Very Much Reduced).—The temporal half of the disk is grayish white, the margins are sharp, the scleral ring is distinct, the lamina is not visible, and the vessels are of normal caliber.

This is a case of atrophy of the papillomacular bundle of the optic fibers. As it occurs through toxic influences (especially alcohol, but also tobacco, stramonium, carbon disulphid, and chloral), 16.5 per cent. of alcoholic subjects and 65 per cent. of patients with alcoholic amblyopia show these changes. Similar changes have been observed in diabetes mellitus and after taking cold. It is important to remember that in 1 per cent. of persons with normal sight a somewhat similar pallor of the temporal half of the disk may be observed.

While in this illustration toxic atrophy of the temporal half of the disk presents the characteristics of a simple atrophy, it may in other cases show certain peculiarities of an inflammatory atrophy (indistinct margins, slight sclerosis of the vessels, as in Fig. 4). Both forms are frequently spoken of as retrobulbar neuritis, from the supposition that the cause of the changes is a retrobulbar optic neuritis. The name, however, is not quite correct, as an inflammation of the optic nerve behind the eyeball may lead to changes in the entire disk, in the form of a simple (descending atrophy) or of a neuritic atrophy.

PLATE 10.



1, Simple atrophy of the optic disk in tabes dorsalis; 2, simple atrophy in embolism of the central artery; 3, pressure atrophy in glaucoma simplex; 4, neuritic atrophy; 5, papillitic atrophy after choked disk in gumma of the brain; 6, papillitic atrophy after thrombosis of the central retinal vein; 7, retinal atrophy from chorioretinitis following prolonged lactation with a probable syphilitic basis; 8, atrophy of temporal portion following retrobulbar neuritis from alcoholism.

EXPLORATORY PUNCTURES AND HARPOONING

EXPLORATORY PUNCTURES

By an *exploratory puncture* we mean the introduction of a fine hollow needle, attached to a test puncture or aspirating syringe, into a diseased area, and a subsequent aspiration in order to examine the character of the tissues, and especially to determine the presence or absence of collections of fluid. In puncture to obtain fluid in subcutaneous edema no aspiration is employed.

SYRINGES FOR EXPLORATORY PUNCTURES

The appropriate syringe is a little larger than the ordinary hypodermic syringe, and is furnished with a longer and rather coarser needle. The hypodermic syringe may also be used if such a large needle be fitted to it tightly. A syringe which contains 5 to 10 cc. of fluid is large enough to furnish adequate aspiration force to withdraw even quite solid fragments of tissue and sufficient fluid for a satisfactory chemical or bacteriologic examination. The essentials for a serviceable exploratory puncture (or aspiration) syringe are the following: The glass cylinder should have a uniform caliber, so that the piston fits accurately. The packing must be absolutely tight, so that if the end be closed and the piston withdrawn, the latter will slip back quickly into its former position by the force of suction. The needle must be fitted on air-tight, so that the same test can be successfully applied after the needle is screwed to the syringe. If the material withdrawn is to be examined bacteriologically, the syringe must be carefully sterilized. This can most easily be done with the glass syringes furnished with a metal piston or asbestos packing, and asbestos piston. The most perfect are furnished with a contrivance for compressing the asbestos packing against the cylinder, so that it can be made as tight or as loose as is desired. The cannulas or needles should be of an appropriate size. This is not always the case with the varieties on sale. They should be 6 to 7 cm. ($2\frac{1}{2}$–$2\frac{3}{4}$ in.) long (not including the connecting portion) and about 1 mm. ($\frac{1}{16}$ in.) external diameter, so that the puncture will be sufficiently large. Such fine needles practically obviate the possibility of any danger.

METHOD OF MAKING EXPLORATORY PUNCTURES, AND THE GENERAL RESULTS OBTAINED

Before each attempt the needle must be carefully disinfected according to the strictest surgical rules. This means that after being used it should be carefully cleansed in water, then boiled for ten minutes and kept in alcohol. If the needle be well nickeled, it is not at all injured by this treatment. After use, the syringe itself is best cleansed and prepared for future use in the same manner. The pistons of syringes with asbestos packing must be loosened by means of the appliance described above before boiling, otherwise they may swell too much. Metal pistons are best removed altogether before sterilization by boiling,

so that the glass of the syringe may not be cracked. In boiling up these instruments it must not be forgotten that to insure perfect sterilization the needle as well as the syringe must be filled completely with water, all air-bubbles being thus driven out. If the needle and the syringe are kept in alcohol, all traces of it must be removed before use by rinsing them out with sterile water, for otherwise serous fluids obtained by aspiration may become clouded by the alcohol and thus lead to erroneous conclusions. Traces of water remaining after rinsing out the syringes must also be removed, otherwise one is never sure whether traces of fluid found after aspiration were present in the syringe before the operation or have been obtained from the tissues.

Much discussion has taken place in reference to the disinfection of the skin which should precede all exploratory punctures. It is well known that a strict and perfect disinfection of the skin cannot be attained even by the methods used in the preparation for major operations (the use of soap, alcohol, sublimate solution, etc.), and, indeed, such disinfection is quite unnecessary for such a small operation as an exploratory puncture. The method which has been used for many years in the author's clinic consists in covering the portion of the skin with a layer of 1 : 1000 sublimate solution by means of a slab, without rubbing the skin at all; the puncture is then made through the skin disinfected in this manner, and after the needle is withdrawn, a drop of the same solution is placed on the puncture hole. In the antisepsis of an exploratory puncture the important thing is simply to introduce a trace of the antiseptic solution into the wound so as to prevent the growth of bacteria into it. The author makes use of an alcoholic solution of the sublimate, though this is less suited for purposes of disinfection than a watery solution. The fact is, however, that it is not at all the author's purpose to disinfect, but simply to have a trace of the sublimate remain in the puncture wound after the alcohol has evaporated; an alcoholic solution is best suited to this end because, as is well known, only such solution will stick to a greasy skin. Thorough rubbing with a disinfecting solution, a procedure that is often recommended, can only have one result: the small epithelial scales detached by rubbing and not perfectly disinfected are driven deep into the skin by the needle. The author even makes it a point to warn his students not to employ this method of skin disinfection. The puncture wound is finally covered with a piece of cotton dipped into a 1 : 1000 watery solution of the sublimate.

The skin should first be stretched tightly and the needle inserted perpendicular to the surface, and not too quickly, so as to avoid any bony parts by slightly altering the direction. During the introduction of the needle we should pay special attention to the resistances met with at the different depths. We are then able to select the appropriate moment for aspiration; this should be when we feel that the needle has passed all obstructions, entered a cavity, and is freely movable laterally. Such palpation with the needle should never be neglected. Sometimes, however, a slight amount of fluid is obtained while the needle seems to be sticking into perfectly solid tissue. We should not desist if we obtain no fluid by aspiration, provided we have good reason to believe that fluid is there. Frequently we have penetrated too far or not far enough, and a sligh push or withdrawal of the needle will be sufficient to obtain fluid. In other cases we withdraw the needle partially and then point it in a slightly different direction. If the aspirating force of the syringe

has been completely spent by the gradual withdrawal of the piston, the latter must again be pushed forward into the syringe after first unscrewing it from the needle, so as not to introduce any air into the tissue. At the same time we must be careful to notice any chance movements which may be imparted to the point of the needle by parts which have been punctured or touched, such as the lungs, diaphragm, liver, spleen, heart. Such movements are of the greatest importance for diagnosis. Furthermore, it pays to note the behavior of the piston during an aspiration which does not yield any fluid. It it can be withdrawn only by overcoming a certain amount of resistance, and if, when let loose, it springs forward again because of the pressure of the external atmosphere, it may be concluded that the needle has entered solid tissue, unless its lumen is obstructed. If, on the other hand (the syringe and connections being air-tight), the piston is found to be easily movable and no fluid enters the syringe, it may be concluded that the needle has entered an air-containing space, such as is found in pneumothorax, the lumina of bronchi, pulmonary cavities, gas-containing abscesses, and the lumina of intestines or of the stomach. However, the air-tightness of all connections must first be made sure of before such a conclusion is justified. If the first puncture be unsuccessful and the examiner be still convinced of the presence of fluid in the vicinity, the procedure should be repeated at an adjoining spot after he has again more carefully examined the locality. If not a drop of pus has been obtained by the first puncture and a severe suppurative infection is not present, the same cannula may be again used in case of necessity. Otherwise, it is best to use a new cannula for each new puncture or to disinfect the old one by boiling before using it again. In every case where we find fluid it is advisable to aspirate a sufficient quantity to perform all the necessary examinations. If the needle enter solid tissue, and we wish to examine this tissue histologically, we can generally obtain a specimen by pulling the needle back and forth a few millimeters, twisting it at the same time so that it acts like a cork-borer. Then with sufficiently strong aspiration we can suck out a fragment of the tissue large enough for microscopic examination. In this attempt the needle must be very carefully withdrawn after the aspiration. Its contents, which often consist of quite small tissue fragments, can usually be forced out upon a glass slide by a vigorous push of the piston. The fragments may then be teased apart and examined microscopically. Whenever, in any exploratory puncture, aspiration brings no fluid, we should never neglect to examine the contents of the needle carefully in the way described. Aspiration frequently obtains only tiny flakes of pus from purulent infiltrated tissue or from thick collections of pus. Such flakes microscopically demonstrated are oftentimes quite sufficient for diagnostic purposes.

If the object be to obtain some fluid from edematous subcutaneous tissues for examination, one of Southey's cannulas, such as are used for therapeutic purposes in treating edema, may be employed. The cannula armed with the stilet is introduced perpendicularly into the skin, and when the stilet is removed, the fluid usually falls drop by drop from the cannula. A small tube may be attached to the latter and the fluid conveyed directly into a beaker.

Where we obtain a large amount of fluid from an exploratory puncture, the first essential always is to examine this fluid macroscopically;

thereby we determine definitely whether it is serous or purulent,[1] clear or turbid, colorless or colored, bloody, bile stained, odorless or foul-smelling, and, if purulent, whether it contains the characteristic granules of actinomycosis. (See p. 724.) In turbid serous fluids the macroscopic appearances are often sufficient to decide between a purulent and a fibrinous turbidity, since the latter is characterized by the presence of flocculi. Otherwise a microscopic examination must be made. This will also furnish information in reference to the so-called chylous character of a fluid, *i. e.*, a turbidity caused by the presence of minute particles of fat. Chylous fluid in a cavity may be due to a number of different causes. As a result of a stasis of lymph in the thoracic duct, the fluid may become admixed with chyle by diapedesis without there being any solution of continuity of the lymph-vessels. In tuberculosis or malignant tumors of the pleura or of the peritoneum the thoracic duct or some of the smaller lymphatic vessels may be ulcerated by the destructive process and the chyle poured out into the affected cavity. In all these cases, as in chyluria, the *admixture with chyle* may be recognized by the microscopic examination of the fluid. The fat is not present in large drops, but in the finest droplets, which in size somewhat resemble micrococci, and usually exhibit the so-called Brownian movement. In addition to the fact that they do not stain well in dry preparations (see p. 715), they may be differentiated from micro-organisms by their great quantity, since such a large number of micro-organisms could scarcely be present in a non-purulent fluid. They also show an additional peculiarity in that they tend to collect in a layer upon the upper surface of the fluid when it is allowed to stand. Chemical tests may also be applied after removing the fat from the fluid by agitation with ether. From a chemical standpoint it should also be noted that amounts of sugar greater than those found in the blood are not to be expected in chylous fluids, since sugar leaves the intestine through the veins and not through the lymphatics. True chylous fluids have also been found in cavities under circumstances which have not yet been explained, there being neither a lymph stasis nor a rupture of a lymphatic. In these cases the serosa is possibly abnormally permeable to fat-particles, which, as is well known, are present in large numbers in normal blood after the ingestion of food. (See p. 811.) These true chylous exudates and transudates are not to be confounded with fluids in which the turbidity depends upon the presence of larger fat-globules. In the latter instance the finding of cells containing fat-droplets demonstrates that the admixture is dependent upon fatty degeneration of endothelial cells or of tumor cells.

Microscopic examination will also give information in reference to the *presence of leukocytes* and *admixtures with blood* which would escape macroscopic inspection (see p. 918 et seq.), and to the presence of cholesterin crystals in old serous exudates (Fig. 278, *b*); it will also reveal the presence of *hematoidin crystals* (Fig. 278, *d*) in purulent collections (pleural empyemata, subphrenic abscesses, pulmonary ab-

[1] Although it seems very simple to differentiate a serous from a purulent exudate by means of exploratory puncture, errors may easily be made, since thin, purulent exudates tend to settle, so that if the puncture be made high up, nothing but a clear serum may be obtained; the pus-corpuscles sink to the bottom of the cavity. In doubtful cases it is consequently advisable to make a second puncture at a lower level.

scesses, and empyema of gall-bladder), and particularly the presence of *bacteria*. Dry preparations should be made. (See p. 715.) It is best to select fibrinous flocculi obtained by centrifugation, for the bacteria are caught in the meshes of the fibrin network. When a serous exudate contains but few bacteria, their discovery may be facilitated by centrifugation in accordance with the method suggested by Ilkewitsch for the examination of sputum for tubercle bacilli. Glacial acetic acid is added to the fluid, and the bacteria settle with the precipitate. In addition to the foul odor, the microscopic demonstration of food-particles and innumerable bacteria in the fluid obtained from the peritoneal cavity by exploratory puncture is of great importance for the demonstration of a perforation of the stomach or intestine. [Exploratory puncture of the peritoneal cavity has been entirely superseded by an exploratory laparotomy.—Ed.] The microscopic demonstration of particles of tumors in fluids obtained by puncture is also of importance. They may be found as isolated cells, differing from the normal endothelium, or as peculiar cell conglomerations, the latter being evidence of a much more positive character.

When a serous fluid is obtained, it is sometimes of importance to determine by the examination of this fluid whether it be an *exudate* or a *transudate* (in cases where the determination is impossible by other means). This may be done by estimating the protein content, determining the specific gravity and the number of leukocytes, and demonstrating the presence of a protein which is precipitated by acetic acid.

The protein contained in the fluid withdrawn is most accurately estimated by weighing the precipitated protein according to the method mentioned upon p. 613. Esbach's method, although reasonably accurate for urinary examination (p. 615 et seq.), is not applicable for serous fluids. If it be used, however, the fluid, rich in protein, should be diluted with urine in order to preserve the relations (specific gravity, salt content) of the usual urinary test. Reiss has recently worked out a method of estimating the protein content of puncture fluids with the aid of Pulfrich's immersion refractometer.[1] (See p. 614.) A great many statements are to be found in literature[2] upon the protein content of exudates and transudates. It is practically agreed that hydropic transudates contain much less protein than inflammatory exudates. Nevertheless, most observers contend that the distinction is not sufficiently sharp, and that the rules are not sufficiently general in their application to permit of a differential diagnosis between exudates and transudates. Runeberg,[3] however, contends very emphatically that the protein content in serous fluid is of distinct diagnostic significance. He believes that the difficulties which have thus far militated against the diagnostic importance of the protein content mainly depend upon the fact that various observers have contrasted merely inflammatory with hydropic effusions, whereas in reality the

[1] Reiss, Brechungsquotient des Blutserums als Indicator für Serumgehalt, I. A. D., Strassburg, 1904; ibid., Arch. f. exp. Path., 1904, vol. li. His tables are printed in Zeiss' prospectus of Pulfrich's refractometer.

[2] Compare, for example, Vierordt, Daten und Tabellen, 1888; Bernheim, Virchow's Arch., vol. cxxxvii, and others.

[3] Von der diagnostischen Bedeutung des Eiweissgehaltes in pathologischen Trans- und Exsudaten, Berlin. klin. Woch., 1897, No. 33.

distinction must also be made between—(*a*) congestion transudates and (*b*) hydremic transudates. Besides, these observers have not heeded the possibility of a combined origin for such effusions. Runeberg's experience shows that the estimation of the protein content of the fluid is very essential in the diagnosis of such combined forms. He determined that the protein content was 4 to 6 per cent. in inflammatory exudates (including tuberculosis and carcinomatosis of the serous membranes); whereas the protein content in pure congestion transudates varied between 1 and 3 per cent., and in pure hydremic transudates, from 0.1 to 0.3 per cent., scarcely ever exceeding 0.5 per cent. These figures are sufficient for the diagnosis of fresh effusions, but to avoid incorrect conclusions it should be remembered that the protein content in old congestion transudates rises under high pressure, where they are undergoing absorption, or where changes in the serous membranes, nearly related to inflammatory changes, are developed as a result of chronic congestions (connective-tissue sclerosis, endothelial desquamation). In such cases we are in reality dealing with combined forms, and their occurrence will explain most of the apparent contradictions to the above-mentioned rules.

These combined forms are naturally much more difficult to diagnose, but, as a matter of fact, the protein content of the fluid really enables us, at least, frequently to analyze clinically such a disease picture, and is especially valuable in the determination of the proper therapy. Alterations of the protein content during the same clinical observation may furnish valuable conclusions. For example, they may suggest the appearance of a carcinomatous peritonitis as a complication of a portal stasis produced by carcinoma, or, again, the addition of congestion to a pure renal hydrops. The great difficulty in the practical application of these important facts is the complexity of an exact quantitative protein estimation; it is too difficult for bedside work. To overcome this difficulty Runeberg has adopted a method which, although it does not measure the protein content exactly, is sufficiently accurate for the purpose in view. He adds a few drops of nitric acid to the fluid in a test-tube, and then judges by the shape and consistence of the precipitate. In exudates which depend upon a local affection of the serous membrane (inflammation, tuberculosis, carcinomatosis) the precipitate forms thick, heavy clumps which quickly sink to the bottom of the glass; in congestion transudates, abundant large flocculi, which ordinarily sink to the bottom also, but which are more loosely and more lightly precipitated; in pure hydremic transudates, merely a decided opalescence or small, loose flakes which float for a long time in the fluid. Evidently a certain personal experience, acquired from sharply defined cases, is essential for correctly differentiating the mixed forms. Runeberg also emphasizes in the differentiation, in addition to the protein content, the precipitation with acetic acid (see below).

F. A. Hoffmann[1] has investigated the protein content of fluid in edema. He found that ordinary edematous fluids occurring in cachexia or stasis usually contain 0.1 to 0.8 per cent., whereas in kidney disease a content of less than 0.1 per cent. was found.

The *specific gravity* of serous fluids is approximately proportional to the protein content, and may, therefore, be utilized for a rough esti-

[1] Hoffmann, Deut. Arch. f. klin. Med., vol. xliv, part 4.

mation of the latter. According to Ruess,[1] the following figures represent the relation between the specific gravity and protein content:

Specific gravity.		Protein content.
1018	higher than	4.0 per cent.
1015	lower than	2.5 "
1012	" "	1.5 to 2.0 "
1010	" "	1.0 to 1.5 "
1008.8	" "	0.5 to 1.0 "

An ordinary urinometer (p. 551) is sufficiently accurate and the most convenient instrument to employ for estimating the specific gravity. A sufficient quantity of fluid is obtained, before the needle is withdrawn, by repeated suction and emptying of the syringe. Providing a fine needle, such as recommended above, be used, the syringe may be disconnected without risk of producing pneumothorax even in pleuritic effusions under negative pressure, because the internal friction of the needle is too great to be overcome by the difference between the latter and that of the outside air. If necessary, the specific gravity may also be estimated from a smaller quantity of fluid by the pyknometric method described for the blood on p. 735, or by Hammerschlag's method, although the latter procedure is more difficult. It is probable that the amount of protein precipitated by acetic acid from a fluid obtained by aspiration depends on the number of leukocytes therein or the quantity of their products of decomposition.

The demonstration of this protein was first shown by Primavera and Rivalta[2] to possess a certain importance for the differentiation between exudates and transudates. An abundance of this protein is evidence in favor of an inflammatory exudate and against a transudate. Rivalta's test is performed in the following manner: An exceedingly dilute aqueous solution of acetic acid (2 drops of glacial acetic acid to 200 cc. of water) is prepared, and a drop of the fluid to be examined is allowed to fall into this solution from a glass rod. If the fluid contain a considerable quantity of the substance in question, the drop immediately sinks to the bottom of the acid solution, producing a turbidity resembling a cloud of cigar smoke. If the questionable substance be absent, no turbidity appears; if present in slight amount, the cloudiness is very slight and of gradual development. Following the suggestion of Paijkull, Runeberg demonstrates the presence of this substance simply by the addition of a few drops of acetic acid to the fluid. In inflammatory exudates a more or less marked turbidity appears, while in transudates this is very slight or entirely absent. The nature of this substance is still under discussion. Rivalta formerly believed it to be nucleo-albumin, but now[3] regards it as a mixture of euglobulin (paraglobulin) and pseudoglobulin. Umber[4] thinks it is a mucin, and designates it as serosamucin, while Stähelin[5] believes that it is related more closely to the globulins than to the mucins. It would seem that the different authors are not working with the same substance, since Rivalta, for example, expressly states that it is soluble in a slight excess of acetic acid, while Umber declares the

[1] See Vierordt, Daten und Tabellen, 1888.
[2] Riforma med., April, 1895.
[3] Policlinico, 1904.
[4] Zeit. f. klin. Med., vol. xlviii, parts v and vi, p. 364.
[5] Münch. med. Woch., 1902, p. 34.

opposite to be the case. In regard to the reaction (Nonne-Appelt) recommended in the case of cerebrospinal fluid, see p. 941.

Another important criterion for the inflammatory origin of a serous fluid is its content of fibrin ferment, which is manifested by the spontaneous formation of fibrin either before or after the withdrawal of the fluid.

The presence of *bile-pigment* in the fluid may also be important, particularly so when the biliary pasages perforate into the peritoneal or pleural cavities. In addition to the characteristic yellowish-brown or greenish discoloration, the reactions for the bile-pigments may be demonstrated by the same methods as those employed for the urine.

For a *bacteriologic examination* of aspirated fluid the culture method is to be recommended in addition to the above-mentioned microscopic examination, because with serous fluids the latter rarely furnishes a positive result. With a purulent exudate, except with purulent tuberculosis, the ordinary stick or streak inoculation frequently furnishes positive results; but with serous exudates, which contain very few micro-organisms, a much larger amount of fluid must be employed for inoculation, just as in the bacteriologic examination of the blood. (See p. 814.) A number of drops, from 5 to 10, may be squirted from the syringe directly into culture-tubes containing slant-agar gelatin or bouillon. Plate cultures may be employed, as is mentioned in the examination of the blood. In regard to the technic, text-books on bacteriology should be consulted.

Gas as well as fluid is sometimes withdrawn in punctures; for example, in abdominal punctures when the point of the needle penetrates the stomach or the intestines, in pyopneumothorax, in pulmonary cavities in case the cannula has entered a bronchus, and in abscesses which contain gas. This finding may have some diagnostic significance, but only when we are sure that the gas was aspirated through the needle and not through a leak in the syringe. (See p. 911 for a method of testing the syringes.)

In addition to the determination of the presence of fluid collections, as well as their peculiarities and characteristics, exploratory punctures are especially important in order to decide upon the spot for attempting therapeutic punctures. Immediately before any therapeutic puncture we should demonstrate the presence of fluid by an exploratory puncture exactly at the spot to be selected, and should demonstrate the free mobility of the puncture needle in a cavity. Otherwise we run a danger of causing some injury in a therapeutic puncture with the coarse and much more injurious instruments, should we penetrate, for example, local adhesions of the lungs or heart, or in abdominal punctures, a full intestinal coil.

THE EXAMINATION OF THE CELLS AND FERMENTS FOUND IN PUNCTURE FLUIDS

(See p. 937, Lumbar Puncture, for description of cerebrospinal fluid.)

A method of investigation rejoicing in the promising title of cytodiagnosis has been introduced by French writers, particularly by Widal and his pupils. It consists of the study of the character and number of the cellular constituents of exudates and transudates, and of subsequent deductions from these studies as to the nature of the fluids.

The sediment obtained by gravity or centrifugation is either subjected to direct microscopic observation, or, when greater accuracy is required, is utilized for the

preparation of cover-glass specimens. Jenner's stain is well adapted for staining such preparations. In such dry preparations the relative numbers of the different varieties of cells may be observed, particularly of the leukocytes. For this purpose the movable stage or Ehrlich's ocular diaphragm (p. 794) may be employed. The absolute numbers may be determined by counting the cells according to the method used in estimating the number of white cells in the blood, the fluid being used undiluted or diluted, as is best in each individual case. (See p. 757.)

If the exudate coagulate rapidly soon after its withdrawal, Widal advises that the coagula be broken up by agitation with glass beads before centrifugation. It is doubtful whether accurate results are obtained by this procedure, since a great many of the cellular elements will always remain embedded in the coagula. Instead of utilizing this procedure, the examiner can prevent the coagulation of the fluid by aspirating it into a syringe half filled with ammonium oxalate solution, sodium citrate solution, leech infusion, or a solution of hirudin. The ammonium oxalate solution consists of 2 parts of ammonium oxalate to 1000 parts of normal saline solution. The leech infusion is prepared by cutting the head of a leech into small pieces and rubbing them up in a mortar with sand. This mixture is then diluted with cold normal saline infusion, allowed to stand for an hour, during which time it is frequently stirred, and finally filtered. Instead of this infusion, physiologic saline solution, to which a small amount of commercial hirudin (1 mg. to a few cubic centimeters) has been added, may also be employed. The employment of these agents preventing coagulation is to be particularly recommended when the sediment is obtained by gravity rather than by centrifugation, since in the necessary interval some of the leukocytes may become disintegrated and be caught in the fibrin network. Instead of preparing dry smears from centrifuged or sedimented puncture fluids N. Jagic has lately recommended the staining of the sediment in the moist state while it is still contained in the centrifuge tube. He uses the Giemsa stain[1] for this purpose. The method employed by him is as follows: After thoroughly centrifuging the fluid that is to be examined,[2] the plasma is poured off carefully and the sediment is shaken in the centrifuge tube with about 10 cc. of 2 per cent. formaldehyd solution. The mixture is then centrifuged once more, and the formaldehyd solution is carefully poured off or removed by a pipet. The sediment is then mixed with about 1 cc. of Giemsa's solution diluted with the same amount of water. The mixing is done by means of a platinum wire, for about five minutes, this period being sufficient for staining, and then a drop of the stained fluid spread on a slide and covered with a cover-glass is examined microscopically. If the stain be not sufficiently deep, 1 or 2 drops of the concentrated Giemsa solution may be added to intensify it. The preparation may be ringed with gum shellac and thus preserved for some time.

The morphologic elements demanding our attention in cytodiagnosis are: erythrocytes, the various kinds of leukocytes, endothelial or epithelial cells, and the cells of tumors.

The microscopic study of the erythrocytes furnishes but little additional information to that obtained by a macroscopic inspection of the fluid. The presence of blood may be demonstrated also by chemical means (for methods employed see section upon Urinary Examination), but the microscopic demonstration is a more refined diagnostic procedure. Large quantities of blood are found in carcinomatous, tuberculous, and nephritic exudates, in the transudates of marked venous congestion, and in all the hemorrhagic diatheses.

The literature[3] of cytodiagnosis is already quite extensive, and the greatest discussion has been in reference to the leukocytes contained in the fluid. It is to be supposed *a priori* that a large number of leukocytes speaks for an inflammatory origin of the particular fluid, and that the number of leukocytes is proportional to the intensity of the inflammation, as may be easily verified by studying the occurrence of suppuration in any serous exudate. Cytodiagnosis, however, has gone much farther, and just as certain blood-pictures have been accepted as characteristic of certain diseases of the blood and hematopoietic organs, definite cytodiagnostic formulas, based upon the nature and relative numbers of the leuko-

[1] See p. 779 et seq. The solution may be obtained ready-made for use from Grübler, in Leipzig.

[2] The addition of solutions to prevent coagulation is likewise advisable. (See above.)

[3] See Brion, Centralbl. f. allg. Path., 1903, vol. xiv, b. 609; H. Königer, Die cytologische Untersuchungsmethode, etc., Jena, G. Fischer, 1908. The latter work contains a detailed review of the literature.

cytes contained in the fluid in a cavity, have been suggested for the diagnosis of the underlying disease process. This is particularly noticeable in the attempts that have been made to differentiate tuberculous exudates, non-tuberculous exudates, and the exudates of malignant tumors, from the relative numbers of the polynuclear and mononuclear elements.

It would seem that these efforts have gone too far, and that the empiric or statistic findings have not been tested by our knowledge of general pathology. Although we know that the emigration of polynuclear leukocytes is one of the essential characteristics of inflammation, it has not yet been decided whether mononuclear cells or leukocytes ever pass out of the blood-vessels. It is generally supposed that by far the greater number of the mononuclear cells are the result of regenerative processes which are associated with and consecutive to the inflammation, and that they originate in the lymphoid tissue which is found disseminated throughout almost all the viscera. In addition lymphocytes derived from the lymph are found in fluids obtained from cavities.

If we abandon the crude empiric or statistic standpoint from which the question of cytodiagnosis is usually considered, and which leads to erroneous conclusions because it does not lay sufficient stress upon the different stages and degrees of the inflammatory process, it would seem that a large number of polynuclear cells is indicative of marked and recent inflammations, while a considerable quantity of mononuclear elements signifies either a milder degree and later stage of an inflammation or the presence of a non-inflammatory process.

In addition to red blood-cells, polynuclear cells, and lymphocytes there are often found in fluids obtained from serous cavities many mononuclear cells that probably represent endothelial elements derived from the serosa. Frequently, these cells still show the typical polyhedral shape, but, on the other hand, they may be degenerated or changed in form and structure because of swelling or shriveling. Usually they are rounded in shape and may be either discrete or in groups and ragged aggregations that have been termed "endothelial plates." Of course, the presence of endothelial cells in these fluids is evidence of desquamation, and may be interpreted as signifying some mechanical or chemical injury to the endothelial layer. But their number should not be used as a measure of the damage done in each particular case. Indeed, it may be that the opposite is more true, that is, the more extensive is the damage of the serous coat, the less cells are found in the fluid obtained from the cavity lined by it. This phenomenon is probably explained by the fact that the more severe chemical injuries to the endothelial cells are accompanied by diminution of the regenerative power in the cells; moreover, in severe injuries layers of fibrin take the place of the endothelial coat or simply cover it up; the endothelial cells, too, are numerically overwhelmed by the lymphocytes and leukocytes which originate from the deeper tissues. As a consequence, a preponderance of endothelial cells is seen especially in the purely hydropic transudates, such as arise in passive congestion or in disturbances of the kidneys, and also in such effusions as are caused simply by mechanical non-infectious factors. Examples of the latter type are found in effusions following trauma and those accompanying tumors, when due simply to the mechanical friction between the tumor masses projecting into the serous cavity and the serous coat of the latter. It is to be noted, finally, that occasionally the endothelial cells show well-marked macrophagic properties, taking up not only bacteria, but red and white blood-cells as well.

In addition to these varieties of cells we must finally mention tumor cells which may be found in fluids that appear in the serous cavities in the presence of tumors. The importance of these is, of course, diminished by the fact that surfaces of tumors do not necessarily shed their cells into the cavities even if the serosa itself be infiltrated by the new-growth. Moreover, it is often mpossible to differentiate with certainty tumor cells from endothelial cells that have undergone various changes.

These general principles of cytology show that in each concrete case we must assume a critical attitude toward the various findings obtained by this method of examination, and place but little confidence in any set of "cytodiagnostic formulæ."

It consequently seems to the author that the predominance of either variety of cell in an exudate is less indicative of the etiology of the inflammation than it is of its stage and severity.

Besides the variations due to different stages of the disease, a great obstacle to the utilization of cytodiagnostic findings is that the fluid obtained by aspiration by no means accurately represents the characteristics of the same fluid within the body and at the moment of its origin. It is well known that the cellular elements of a fluid may be so influenced by sedimentation within the body that a serous fluid may be obtained by exploratory puncture, although a complete evacuation of the accumu-

lation might demonstrate its purulent character. (See foot-note, p. 914.) Since the various kinds of leukocytes sediment with different degrees of rapidity dependent upon their variations in size, it follows that we cannot always depend upon their relative numbers as determined by a study of the evacuated fluid. The excessive formation of fibrin may also modify the findings, as a variable number of leukocytes are required to produce coagulation and still others are caught in the fibrinous masses, and it is by no means necessary that all varieties of the leukocytes should be implicated in the same proportions.

All these reasons lead the author to regard the conclusions obtained by cytodiagnosis as very deceptive, and to state that they should never be employed as the sole foundation of a diagnosis. In his opinion the establishment of rigid cytodiagnostic formulæ is as much opposed to our knowledge of general pathology as it is to the first commandment of clinical diagnosis—that we should diagnose from all the symptoms and never from a single one. Cytodiagnosis, like many other modern methods of investigation, rejoices in a loud-sounding title, which causes us to forget that it has to do only with the establishment of a single symptom, and it has consequently awakened false hopes which will never be realized. These conclusions have been forced upon the author both by his own experience and also by the contradictory results obtained by means of cytodiagnosis as they have been published

In considering the cytologic findings obtained in the examinations of various cavity fluids, it must, therefore, be remembered that numerous exceptions to the usual types may be present. In a word, there is not a single cytologic picture of these fluids that can be regarded as pathognomonic for any one type of disease.

The Cytology of Fluids Obtained from Serous Cavities

(For the cytology of cerebrospinal fluid see p. 939.)

The main object of controversy in the literature is still the cytologic character of the exudates in so-called primary tuberculous pleurisy. Originally the predominance of lymphocytes over the polynuclear cells was looked upon as the characteristic and almost pathognomonic finding. This assertion, however, could not be accepted as it stands, because many exudates that contain lymphocytes exclusively are not tuberculous, and, on the other hand, quite a number of quite recent tuberculous exudates contain an abundant, indeed, an overwhelming, number of polynuclear cells. Königer states, however, that even in these cases the lymphocytes begin to predominate after the second week, replacing the polynuclear cells as well as the endothelial cells which, though present in large numbers early in the case, gradually disappear. Evidently, such predominance of lymphocytes depends upon the relatively benign character of the so-called primary tuberculous pleurisy. In these cases the real inflammatory phenomena disappear very quickly, and the tuberculosis, which in itself cannot be looked upon as an inflammatory process, leads to a hyperplasia of the lymphatic tissue. However, there are exceptions to this behavior of tissues if the tuberculous pleurisies are of higher virulence; in this case polynuclear cells predominate for a longer time. On the other hand, it must be admitted that exudates of a different type may present cytologic pictures similar to the tuberculous exudates, with their abundance of lymphocytes, if the infection causing them is of the same degree of virulence as in tuberculosis. The predominance of polynuclear cells for a longer period of time has been regarded as characteristic of the so-called secondary tuberculous pleurisy, that is, for such cases as develop on top of a manifest tuberculosis. The author, however, cannot grant that this differentiation is justified by the facts. Even the so-called primary tuberculous pleurisy is, of course, not primary in the real sense of the word, depending, as it does, upon the existence of tuberculous foci elsewhere in the body. A certain diagnostic importance must also be attached to the presence of red blood-cells, which are frequently, though not at all constantly, found in these fluids. However, any type of pleurisy may lead to the appearance of a hemorrhagic exudate. Königer lays special stress in diagnosis upon the character of the polynuclear cells, which, if exceptionally numerous in a tuberculous pleurisy, usually degenerate very quickly. They either shrivel, the nuclei becoming pyknotic, or they simply break up. The resulting structures are peculiar small cells which occasionally resemble the neutrophile pseudolymphocytes described on p. 792. To be sure, the neutrophile granules often disappear in this process of degeneration, and the cells may then be mistaken for lymphocytes or for nucleated red blood-cells. Fig. 3 Pl. IX, shows such pseudolymphocytes or dwarfed leukocytes that were present in abundance in a tuberculous pleural exudate. The tuberculous nature of the exudate was in this case made sure by the finding of tubercle bacilli

in the fluid. The very abundant content in endothelial cells was also quite striking in this case; they were found either discrete or in large strips and "plaques," appearing in a great variety of forms. The patient suffering with this affection was finally cured. Königer's claim that the absence of endothelial cells differentiates tuberculous exudates from transudates in nephritis and in passive congestion possessing the same cellular content so far as the lymphocytes are concerned cannot be reconciled with the findings in this remarkable case, which, until tubercle bacilli were discovered in the exudate, was supposed to be a malignant tumor of the pleura.

Similar findings characterize the exudates accompanying tuberculous peritonitis.

The exudates due to acute infections (streptococcic, staphylococcic, pneumococcic, typhoid, or rheumatic fever) usually contain, in the early stages, at least, a preponderance of polynuclear leukocytes, even when they are not frankly purulent in character. Königer thinks that it is typical for the leukocytes in these cases to degenerate by the swelling and hyaline changes of the cell-body and of the nucleus, by the appearance of vacuoles in the former and by the diminution of the chromophilic property of the protoplasm and of the nucleus. These processes differ from those occurring in the degeneration of the polynuclear cells in tuberculosis, and are thus important from the standpoint of differential diagnosis. In later stages of these affections also the polynuclear cells may be replaced by lymphocytes. In cases of pleurisy due to infarcts only polynuclear cells likewise predominate in the early stages; later they are replaced by lymphocytes.

Hydropic exudates, usually due to passive congestion or to affections of the kidneys, are characterized in general by the abundance of endothelial cells, that are cast off singly or in plates. Lymphocytes are likewise numerous, while in uncomplicated cases polynuclear leukocytes are not seen at all. Red blood-cells are found frequently in transudates due to passive congestion as well as in effusions accompanying nephritis.

When pulmonary infarctions take place or symptoms of uremia are present, polynuclear leukocytes frequently appear as well. Paracenteses may likewise lead to such secondary changes in the character of the fluids. Serous effusions accompanying neoplasms are generally characterized by their abundant content in endothelial cells. Tumor cells likewise may be present. The latter, however, are often extremely hard to differentiate from endothelial cells. Extreme degeneration, especially of fatty nature, has been claimed to be characteristic of tumor cells, yet one would be very venturesome to base a diagnosis of a tumor on this phenomenon. Occasionally, however, larger particles of tumor tissue may be found in puncture fluids. In such a case the advanced degeneration of the cells and the stratified structure of the cell groups should have some weight in the microscopic diagnosis of such particles as tumors; in other cases certain forms of cells characteristic of individual types of tumors, especially if such cells occur repeatedly in large collections, are of importance in differentiating tumor tissue from the endothelial cells that are usually roundish in form. Among such forms cylindroid cells, spindle-shaped cells, etc., may be mentioned.

A rather infrequent and peculiar phenomenon is the occurrence of many eosinophile polynuclear cells of pleuritic exudates—the so-called "pleural eosinophilia" of the French authors. Such cells may occasionally reach 75 per cent. of all the cellular elements present. On the other hand, smaller numbers of eosinophile cells, ranging from 1 to 5 per cent. of the total number, is quite a frequent finding. Up to the present time all attempts to determine the significance of well-marked eosinophilia of the pleuritic fluids have been unsuccessful. The circumstances under which these cells make their appearance are quite varied. They have been found in tuberculosis, in the exudates of polyarthritis, in pulmonary gangrene, in the presence of malignant tumors, etc., so that no pathognomonic significance can be attached to them. In such cases pleural eosinophilia is quite independent from the conditions in the blood which does not necessarily show a similar predominance of eosinophile cells at the same time.

Finally, the occasional more or less marked predominance of mast cells in pleural exudates must be mentioned; the significance of these cells, however, has been no more securely determined than that of pleural eosinophilia.

Cytology of Purulent Exudates

Only a few studies of this subject exist, apparently because suppuration is regarded as one and the same condition in every case, though it is probable that such a view is not justified. The most important problem is the differentiation of tuber-

culous purulent exudates from such as are caused by the common pyogenic organisms, staphylococci, streptococci, etc. As we have seen, the degeneration of the polynuclear cells, with their transformation into pseudolymphocytes or dwarfed leukocytes, is typical of the serous tuberculous exudation. On the other hand, in a purulent tuberculous exudate the cells usually undergo complete granular and fatty degeneration, so that in a tuberculous empyema of the pleura, for instance, after a while only nuclei and detritus are found. Finally, in an acute suppurative non-tuberculous empyema, the pus-cells are either perfectly preserved or, if the disease has lasted a long time, they degenerate in quite a different fashion. Instead of extensive degeneration, the cell and the nucleus appear simply swollen and poorly stained, just as in serous exudates of a similar nature. In general it may be said that the leukocytes of exudates due to acute infections are the better preserved the milder the affection. It may be added that tubercle bacilli are found only in the minority of cases in tuberculous pus; in most cases such pus appears to be sterile microscopically, even if it prove virulent by inoculation into animals. In other purulent processes the causative agents are usually found in the dry preparations without very much trouble.

Proteolytic Properties of Exudate Cells

H. Kolaczek and E. Müller[1] have described a method for differentiating chemically pus caused by pyogenic cocci from tuberculous pus. This method depends upon the presence of distinct proteolytic properties in pus produced by pyogenic cocci, while no such properties are to be found in tuberculous pus. These authors make use of the serum plate method described in the section on the examination of feces for ferments. (See p. 542.) Several drops of the pus that is to be examined are placed on the serum plate, which is then kept at a temperature of 50° to 60° C. The proteolytic action is shown by the liquefaction of the coagulated serum in places where the drops of pus sink into the medium and form small depressions in the plates. Müller and Kolaczek have come to the following conclusions as a result of their investigations:

1. In this test the absence of digestion of the coagulated blood-serum excludes acute suppurative conditions due to the common pyogenic organisms. According to all observations up to the present time, such a result indicates almost surely the tuberculous nature of the process in question. Even in case a very weak proteolytic action is observed, the latter process is probable.

2. Extensive and speedy digestion of the coagulated blood-serum speaks either for an infectious process, caused by the common excitants of acute pyogenic processes, or for tuberculosis plus a mixed infection with such organisms. This phenomenon, however, may also be observed in cases of pure tuberculous infection if the lesion has been previously treated by iodoform injections.

E. Müller has recently shown that the serum plate method can be replaced by a purely chemical reaction with Millon's reagent, which usually gives similar results. This reaction depends upon the ability of Millon's reagent to coagulate proteids, the coagulation being different in character if, in the one case, the pus contain true protein, or, in the other, its chief content be in albumoses resulting from the presence of proteolytic ferments. Müller gives the following description of his method of examination: "Several very small and fairly deep porcelain dishes are filled almost to the top with Millon's mercurial solution. (See p. 604, note 1.) Very different results are then obtained when a drop of thin pus free from blood, obtained from a tuberculous lesion or from one caused by the common pyogenic organisms, is added to the reagent. The drop of pus caused by the pyogenic cocci forms a spreading disc upon the surface of the reagent, while the tuberculous pus is gathered into a firm film. If an attempt be made to lift the first drop with a platinum needle or to depress it, it breaks up very easily. The tuberculous pus, on the other hand, has such a firm consistence that it can be raised out of the fluid without much difficulty, and frequently assumes a bean or pea-shaped form when depressed into the reagent. A few minutes later, or at most within half an hour, another easily noticed difference may be observed. The fluid about the tuberculous pus retains its original color, showing a great contrast to the brilliant red imparted to Millon's reagent by the pus of pyogenic cocci. In a short time the latter color changes to yellow. In both cases, however, the drops of pus that float about in the reagent assume a reddish tinge." Müller thinks that the red discoloration is causes by the presence of aromatic bodies.

[1] See Müller and Jochmann, Cong. f. inn. Med., 1907.

Müller has likewise proved that by means of the serum-plate method proteolytic properties may be shown in the blood of myeloid leukemia, in contradistinction to lymphoid leukemia, thus proving that this property depends upon the presence of myeloid cellular elements. However, the polynuclear cells contained in tuberculous pus are likewise of myeloid nature, and it is quite uncertain, therefore, what causes are responsible for the disappearance of the proteolytic action of such pus. It may be that this action is inhibited by an antiferment, or the ferment itself may have been destroyed.

E. Müller[1] has recently studied the proteolytic properties of the sediments obtained from serous exudates by centrifugation. He has found that in them the proteolytic action was likewise dependent upon the presence of polynuclear cells. The fluid itself, after being freed from the leukocytes, occasionally showed similar activity, due probably to the elements derived by the solution of cells; often, however, such fluid inhibited proteolysis by virtue of its content in antiferment. In this latter respect it was similar in action to normal blood-serum. The final action of such a fluid depends upon the relative quantities of the ferment and antiferment bodies present.

ANIMAL EXPERIMENTS WITH EXUDATES

Animal inoculations for determining the etiology of inflammatory exudates have been confined mostly to the demonstration of tuberculosis. As is well known, tubercle bacilli are found only in a small minority of serous and even purulent tuberculous exudates. This is evidently due to the fact that the bacilli reach the exudates in small numbers only, being, for the most part, retained in the serous membrane itself or in the fibrin layers formed upon it. It may be, too, that the bacilli in these cases assume the granular or split forms that are hard to recognize, or perhaps they lose their acid-fast properties. In such case, just as in the examination of sputum and urine, animal inoculations must be used for a final diagnosis. This method has shown that a great number of so-called idiopathic pleurisies, following a cold, etc., are really of tuberculous nature. However, the statistical data as to the frequency of successful animal inoculations in this type of cases vary very markedly. This is in all probability due to the different technic used by the various observers. The most important element in achieving success in such inoculations consists in the employment of a large quantity of the exudate, the necessity for this being evident from the small content of such exudates in bacilli. At least 10 cc. of the serous exudate should be used in inoculating a guinea-pig, and still better results are obtained when 20, 30, or even more cubic centimeters are used. Such large quantities of exudate may, however, have a toxic effect upon the guinea-pig, which is the only type of animal that comes into consideration in these experiments. The animals may succumb to the toxic effect before the tuberculosis has had time to develop, and, it is, therefore, best to centrifuge serous exudates and use only the sediment which contains most of the bacilli entangled in the fibrin flakes and in the clumps of leukocytes. In this manner it is possible to obtain for injection the virulent portion of 50 cc. of the exudate. For other technical points in reference to the technic of animal inoculations see p. 714, dealing with the examination of sputum.

[Despite Professor Sahli's logical objections to the clinical value of cytodiagnosis, the editor inserts in the following a note which was prepared by Dr. Musgrave for the translation of the last edition:

DIAGNOSTIC VALUE OF PLEURAL FLUIDS

In recent years many investigators in Europe have done a large amount of work with reference to determining the cause of pleural effusions, and two new and valuable methods of investigation have been published.

In 1900 Widal and Ravaut published the results of their researches, based upon the differential enumeration of the white blood-corpuscles and endothelial cells found in the sediments of serous fluids, and, as a result, have formulated the following laws, or so-called cytologic formulas:

1. A predominance of lymphocytes means a tuberculous effusion.
2. A predominance of polynuclear leukocytes means an effusion of an acute infectious origin.
3. A large number of endothelial cells, occurring especially in sheets or plaques, means a mechanical effusion or transudate.

They also divide tuberculous pleurisy into two classes: the primary form,

[1] Deut. Arch. f. klin. Med., 1907, Bd. xci.

in which there are no discoverable lesions of the lungs, and the secondary form, resulting from an underlying tuberculous lung focus.

In the secondary variety the lymphocytic formula, as seen in the primary form, does not usually hold good, but, instead, the sediment is almost entirely composed of necrotic cells and detritus. Of the distinguishable cells, a large proportion

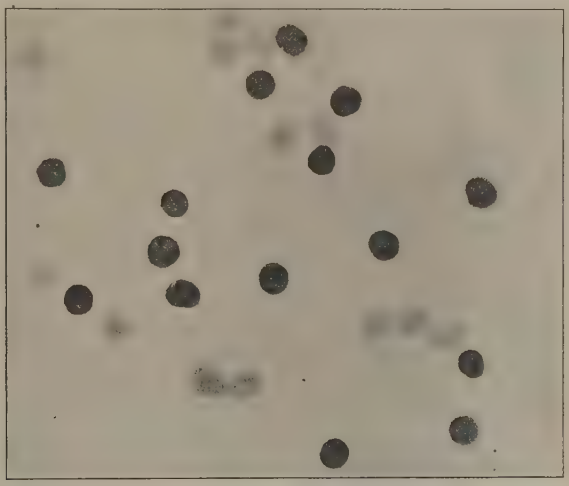


Fig. 359.—Lymphocytosis: Case of primary tuberculous pleurisy (Percy Musgrave; photographed by L. S. Brown).

may be polynuclear. This difference is probably due to a mixed infection. Of the acute infectious varieties, they note those due to the pneumococcus, streptococcus, and staphylococcus. In the pneumococcus variety they described the occurrence of considerable numbers of large cells having phagocytic properties.

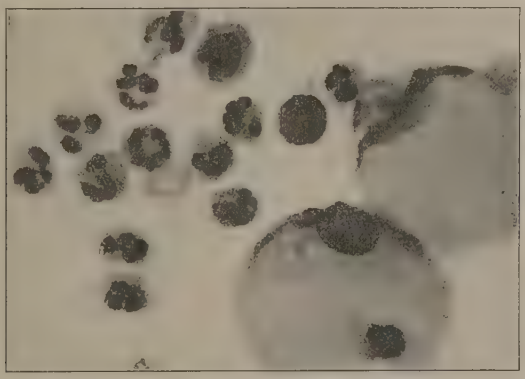


Fig. 360.—Acute infectious pleurisy, showing polynuclear leukocytes and large phagocytic endothelial cells (Percy Musgrave; photographed by L. S. Brown).

In the streptococcus variety these cells are comparatively few in number, and the percentage of polynuclear leukocytes is greater.

These formulas have been extensively investigated by numerous observers, especially in France, and to a lesser extent in Germany, and have, in the main, been found correct. Certain modifications, however, must be taken into consideration.

The chief of these modifications, which has been pointed out especially by Naunyn, is that lymphocytes may also predominate in transudates of long standing or near the end of an acute infectious case where the process is subsiding or where the infection is a very mild one. The specific gravity and the amount of albumin aid us in eliminating the first mentioned of these conditions, and the clinical evidence usually gives a clue to the nature of the process in the second. Both of these conditions are rarely met.

In the first week or ten days of a tuberculous effusion polynuclear elements may predominate, but these rapidly disappear and give place to a purely lymphocytic formula.

The phagocytic cells mentioned above as occurring especially in the cases of pneumococcus origin are of very large diameter as compared with the other elements occurring in the sediment, and the writer has frequently found that they measure as much as 20 μ. These cells frequently contain partly digested polynuclear and other cellular elements, which can easily be seen included in their protoplasm. Their occurrence in large or increasing numbers is usually a good prognostic sign; and their absence, together with the presence of bacteria, is usually a warning of approaching empyema. From the observations which the writer has been able to make, the presence of polynuclears in a proportion of over 90 per

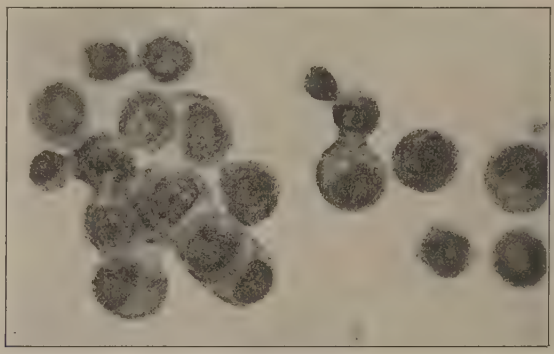


Fig. 361.—Endothelial cells from a pleural transudate due to cardiac disease (Percy Musgrave; photographed by L. S. Brown).

cent., and the presence of bacteria in most cases, precedes an empyema by only a few days.

Little need be said of the formula for the transudates except that the diagnosis is occasionally complicated by the presence of a considerable amount of blood, which raises the specific gravity and the amount of albumin. This blood is usually accidental.

In addition to these three classes of fluids we have the cancerous cases. These are difficult to diagnose, since the majority of pathologists agree, the writer thinks, in saying that it is difficult to differentiate the so-called cancer cells from endothelium, unless actual pieces of the cancerous tissue can be isolated. The iodin reaction (showing glycogenic degeneration) was thought at one time to be suggestive of the cancer cells, but this reaction is very commonly seen in the endothelial cells of simple transudates and in other conditions where endothelium is found.

The few cases of cancer that the writer has been able to study have shown a high specific gravity, 1018 or over, and an albumin content of over 1.5 per cent. The sediment has shown many more endotheliat cells than are found in the tuberculous cases, and these cells are often found in plaques, which is very rare in tuberculosis There is usually a much larger number of lymphocytes proportionally than in the simple transudates.

In addition to the above method of investigating pleural fluids, to which the writers have given the name cytodiagnosis, Jousset has published a new procedure for the detection of tubercle bacilli in these fluids, to which he has given the name of inoscopy, and which is of value in some cases.

The **technic of cytodiagnosis** is as follows: The fluid should be drawn with the usual aseptic precautions into sterilized flasks or tubes. If it is already clotted when received for examination, it should be shaken and stirred with a glass rod until the clot is thoroughly contracted, and the clot, or all clots of large size, should be removed. This is necessary because some of the cellular elements are entangled in the fibrinous meshes, and by contraction of the clot are set free. Widal and Ravaut accomplished the process of defibrination by placing sterilized glass pearls in the flask and shaking the fluid thoroughly. This the writer does not believe is essential for an accurate differential estimate of the cellular elements. The fluid is then placed in centrifuge tubes and centrifugalized for five minutes, at least. The supernatant fluid is decanted gently at first, and when only a small amount remains, the tube is inverted for a few seconds. A few drops will adhere to the side. The sediment is stirred thoroughly with a small platinum loop, the sides of the glass being rubbed to remove adherent portions. When the sediment is thoroughly mixed with the few drops of fluid remaining after decantation, a drop of the mixture is removed with the platinum loop, and a cover-slip smear made. This is allowed to dry spontaneously or by gently heating the preparation. (Heating to the boiling-point will spoil it.)

Many methods of fixing and staining these preparations have been used by the various investigators. Alcohol, ether, chloroform vapor, and osmic acid have been used as fixative agents. Ehrlich's triple stain, hematoxylin and eosin, methylene-blue and eosin, Löffler's blue, and a great variety of other stains have been employed. Some writers have maintained that careful differential staining is not necessary, but from the writer's observations he cannot agree with them, for the reason that careful differential staining of the protoplasm and granules of the polynuclear elements is essential, since the nuclei of these elements are often globular when the cell is degenerated, and they may be mistaken for lymphocytes.

The method of staining which has given the best results in the hands of the writer is practised as follows:

Cover the preparation with a staining fluid composed of:

Wright's blood-stain	3 parts
Pure methyl-alcohol	1 part.

Allow this mixture to remain on the preparation twenty to forty-five seconds, then dilute it with 8 or 10 drops of water, and allow it to stand one to two minutes. Wash very gently, preferably by flooding the slide with a dropper. Do this four or five times, allowing the water to remain on the slide a few seconds each time. Vigorous or forcible washing will destroy the film and spoil the preparation. Dry the preparation by holding it between the thumb and forefinger and waving it through the Bunsen or alcohol flame. Do not attempt to blot the preparation or heat it above the temperature which the fingers will bear. Mount in xylol balsam and examine with an oil-immersion lens.

Inoscopy is practised as follows:

1. The fluid should be drawn with aseptic precautions into sterilized flasks (Erlenmeyer flasks preferably). At least 100 cc. should be taken, although results may sometimes be obtained with much smaller amounts. Allow the fluid thus taken to clot.

2. Shake the fluid gently to contract the clot as much as possible and then wash it, on a piece of sterile linen or fine gauze wrapped over the end of a funnel, until all serum is washed away.

3. Remove the clot or clots with a sterile spatula, and place them in a small flask with sufficient of the following fluid to digest them:

Pepsin	2 gm.
Pure glycerin,	
Strong HCl	of each 10 cc.
Sodium fluorid	3 gm.
Distilled water	2000 cc.

The necessary amount of this fluid will vary, of course, with the size of the clot to be digested, but in most cases 20 or 30 cc. are sufficient. A freshly prepared pepsin (HCl solution) apparently serves as well as the above fluid, but will not keep on standing as the above fluid does.

4. Place the above preparation in the incubator or oven until the clot is digested. A temperature of 37° C. for two or three hours will suffice, but the time is shortened if it is kept at a temperature of 50° C.

5. When the clot has disappeared, pour the mixture into centrifuge tubes and centrifugalize for five to ten minutes. Decant the supernatant fluid as described under Cytodiagnosis.

6. Make a cover-slip preparation and stain it for tubercle bacilli. Care, however, should be taken not to decolorize too long—one-half to three-quarters of a minute with Gabbett's solution is sufficient. Dry and mount.

The majority of the bacilli found by this method are shorter and broader, as a rule, than the tubercle bacilli usually seen in sputum, and some are paler red, but all forms occur. These bacilli may occur singly or in groups. The largest part of the sediment consists of undigested nuclei and a small amount of detritus.

Observations[1] made by the writer at the laboratory of the Massachusetts General Hospital on 72 cases examined with reference to physical properties, albumin, animal inoculation, inoscopy, and cytodiagnosis resulted as follows: 51 cases were classed as tuberculous; 46 of these were classified as primary and 5 as secondary (bacilli in the sputum). Of the 46 secondary cases, 50 per cent. (23 cases) were proved tuberculous by one or more tests, viz., guinea-pig inoculation, inoscopy, or operation. Animal inoculation was positive in 15 cases (32 per cent.), and inoscopy in 10 out of 22 cases examined by this method. One case was proved at operation. In 5 of the 23 unproved cases the examination of the fluid probably led to faulty conclusions. There were 12 acute infectious cases, all showing a predominance of polynuclear leukocytes. Six followed pneumonia, 1 infection of the lung, 3 started from unknown sources, 1 from trauma, and 1 from abscess of the liver. There were 5 cases of simple transudate: 4 due to cardiac disease and 1 to nephritis. There were 3 cancerous cases: 2 positive and 1 doubtful, all following cancer of the breast.

As a result of the study of this subject the writer thinks that we are justified in coming to the conclusion that routine and systematic examination of pleural fluids will aid us greatly in diagnosis and in determining the etiology of pleurisy. Of the methods of which he has spoken, cytodiagnosis is the only one which can easily be employed clinically. Animal inoculation, inoscopy, and culture methods can be employed only in the laboratory. Cytodiagnosis is not accurate in every case any more than any other clinical method, but the writer thinks he is justified in saying that it is sufficiently accurate, especially when taken in conjunction with the history and bedside examination, to justify its use as a routine procedure. In some cases it has not only been of more than probable diagnostic value, but has given us positive and signal results. Routine exaimnation of pleural fluids will not only enable us to study the question of pleurisy with effusion with reference to etiology and diagnosis, but will establish a basis upon which accurate prognostic statistics can subsequently be based.—Percy Musgrave.]

OSMOTIC PRESSURE OF FLUIDS OBTAINED BY PUNCTURE

The osmotic pressure of these fluids is obtained in a manner similar to that employed for the blood. (See pp. 662 et seq. and 845.) This method of study has not yielded practical results. Ketly and Torday[2] state that exudates and transudates cannot be differentiated by variations in their osmotic pressure. It may be said, however, that the lower the osmotic pressure of an exudate or transudate as compared with that of the blood, the greater is the likelihood of the speedy absorption of the fluid. In reference to the freezing-points of these pathologic fluids, it may be stated that they are exceedingly variable, and may be far above or below that of the blood. This is due not only to the initial differences in the character of the particular fluids, but also to the different stages of osmotic interchange at which they are examined.

DETAILS OF EXPLORATORY PUNCTURES IN DIFFERENT DISEASES

EXPLORATORY PUNCTURES OF THE PLEURA

The most important rule for exploratory as well as for therapeutic puncture of the pleural cavity is to avoid introducing the needle too near the upper or too near the lower border of the fluid. If we puncture too low, the needle frequently only goes through both layers, bounding the pleural complementary sinus, these being stuck together with fibrin. If we puncture too high, we are apt to penetrate the

[1] Trans. Mass. Med. Soc., 1904. [2] Arch. f. klin. Med., vol. lxxix.

compressed lung, for the latter often causes a dulness above the level of the fluid. Naturally, there are no generally applicable rules for the place of exploratory puncture, but we must follow the results of physical examination and puncture at a point where we find decided dulness, diminished or bronchial breathing, and diminished fremitus. Generally speaking, however, in typical pleural exudations we select the fifth or sixth intercostal space in the anterior axillary line, or else the area just below the angle of the scapula. In a test puncture of the pleura it is especially important to palpate carefully by moving the needle up and down, and so determine by its mobility whether it has penetrated a large cavity, in order that we may be enabled to select the best spot for a therapeutic puncture or for the drainage of a pleural empyema, and so avoid penetrating the lung or the diaphragm. (See the following in regard to the distinction between pleural empyema and pulmonary abscess.)

The diagnosis of pneumothorax, supported by the results of a physical examination, can sometimes be corroborated by an exploratory puncture. But the aspiration of air is not the only finding to be considered in this case, for air may be obtained not only from the pneumothorax, but also from a bronchus. On the other hand, the complete mobility of the needle in the air space ("palpatory puncture") is the determining factor in the diagnosis of a pneumothorax, whereas the aspiration of air mixed with a mucous secretion shows that the cannula has entered the lumen of a bronchus.

Intrapleural Pressure and Its Measurement in Pleural Exudates and in Pneumothorax

The pressure of a pleural exudate is determined by connecting the cannula used in the exploratory puncture with a water manometer; it is still easier and simpler to use the tube which connects the cannula with the apparatus for the reception of the exudate as a manometer by raising its open end, after it has been filled with the exudate, until the fluid ceases to escape from it. Then the height of the tube above the level of the puncture is measured in centimeters. If the end of the tube must be depressed below the puncture hole to allow the exudate to escape, the figures obtained indicate negative pressure; if it must be raised above it, the figures indicate the positive pressure existing in the pleural cavity.

The pressure of a pleural exudate depends upon two factors, one being the hydrostatic pressure of the column of fluid reaching from the opening of the cannula to the upper level of the fluid, the other the tension exercised upon the fluid by the tissues surrounding it. If D stand for the total pressure, h for the hydrostatic pressure at the level of the cannula, and s for the tension exercised by the tissues containing the exudate, then

$$D = h + s.$$

If the mechanical relations existing in the pleural exudates are to be analyzed, the values h and s can with ease be estimated separately. The hydrostatic pressure by the definition is equal to a column of fluid of the same height as the distance from the site of the puncture to the highest level of the fluid. This distance can be estimated directly in centimeters from the data of the physical examination. As only slight differences exist between the specific gravity of the various exudates and that of water, the figures obtained give accurately enough the hydrostatic pressure measured in terms of a column of water. If, now, this value be subtracted from the total pressure obtained manometrically at the site of the puncture, the tension pressure, which may be positive or negative, is obtained. The tension pressure may likewise be measured directly by determining how far the level of the fluid in the ascending branch of the manometer rises above or sinks below the level of the fluid in the thorax, as determined by the physical examination. It is to be remembered that the level of the puncture is not used in this determination. If the aspirating tube be used instead of the manometer, the level which its open end must reach just to allow the escape of the fluid is used as the point of measurement. If the level of the mouth of the tube or of the fluid in the manometer be above the level of the fluid in the thorax, the tension pressure is positive; if it does not reach that level that element of the total pressure is negative. Both methods, of course, depend upon one and the same principle, as will be seen from a graphic representation of the above equation, and their results agree with each other. D. Gerhardt used the latter method, while the same values are determined in the author's clinic by means of subtracting the value for the pressure of fluid from the general pressure as explained above.

D. Gerhardt[1] has properly called attention to the fact that the usual statements concerning the positive pressure of pleural exudates have reference only to the total pressure. If the tension pressure alone, *i. e.*, the total pressure minus the hydrostatic pressure of the fluid, be considered, it is found to be, in the majority of cases, a negative quantity, even when a recent large exudate causing marked dyspnea is present. The figures for negative pressure obtained in these cases range, according to Gerhardt, from —2 to —20 cm. of water. This phenomenon is in part explained by the compression of the lung through the increasing exudate if the former has not been rendered incompressible by adhesions or by infiltration. This factor, however, explains only why the pressure in question does not necessarily overcome atmospheric pressure, that is, is not necessarily a positive quantity. The negative figures obtained for the tension pressure, on the other hand, are explained by Gerhardt's experiments. He found that when the pleural cavities of a dog were being gradually filled with an increasing quantity of fluid, the tension pressure after a temporary rise rapidly sank to the normal negative values; it became permanently positive only in the presence of large amounts of fluid, which led to urgent dyspnea, rapidly terminating in death if relief were not given. Gerhardt explains these findings by assuming that with the increase of fluid in the pleural cavity the animal, urged on by the stimulus of suffocation, expands its thorax more and more, tending to hold it in the position of inspiration. He thinks that the same thing occurs in the formation of a pleural exudate, so that in spite of the dyspnea or, as Gerhardt puts it, because of the dyspnea, not only the tension pressure, but even the total pressure, may remain negative, however large the amount of the fluid in the pleural cavity may be. This useful drop in the pressure is produced by the increase in the capacity of the sound side of the chest, with its increased respiratory excursions, as well as by the expansion of the affected side. The marked expansion of the healthy side of the chest accounts for the dislocation of the heart, even if negative pressure accompany the presence of the exudate, because the diminution in pressure produced by the marked respiratory movements of the healthy side may often be greater than in the affected pleural cavity. Of course, the displacement of the heart is likewise favored by the positive element of pressure, the hydrostatic factor, which exists only on the affected side of the chest. It is this negative total pressure of exudates that makes simple puncture of the pleural cavity without the use of an aspirating apparatus dangerous. The danger, which the author has often pointed out in his clinical lectures, may be present even in the case of recent large exudates. The puncture hole may give access to air, which rushes in because of the negative pressure, and an artificial pneumothorax be thus produced. This accident is especially liable to happen if a high intercostal space be selected for the exploratory puncture, so that the diaphragm may be surely avoided. At such levels the positive element of the pressure, the hydrostatic effect of the column of fluid, is less apt to overcome the negative element, the tension pressure of the tissues containing the exudate. It must not be forgotten, either, that even if the total pressure be positive in the expiratory phase, it must of necessity always become negative in the inspiratory phase, if the lung be not at a complete standstill because of the exudate; otherwise no breathing is possible. Hence the well-known but occasionally neglected rule, always to precede an exploratory puncture of the pleural cavity by setting the aspirating apparatus at work and continuing suction at least until the tube for the escape of the fluid has become completely filled. After the latter has been accomplished, the suction may be stopped, if care be taken not to raise the mouth of the tube, which now acts as a siphon, any higher than the level at which the fluid still escapes from the pleural cavity.

Of course, the circumstances which favor the formation of a negative pressure in the presence of a pleural exudate are modified if, instead of soft and elastic walls, the space containing the exudate be inclosed by firm adhesions, or if the lung has become inelastic because of infiltration. In such a case even a moderate exudate may lead to the formation of positive pressure as high as its uppermost level. But this is simply a local phenomenon, while the intrathoracic pressure beyond the limits of the exudate may not be affected at all or may sink because of the effects of dyspnea, as Gerhardt has shown. The presence of a localized positive pressure need not, of course, interfere at all with the respiratory function of the affected side of the chest, even though this pressure remain positive during the inspiratory phase.

Of course, a different condition of affairs is present in an open pneumothorax,

[1] D. Gerhardt, Deut. Arch. f. exp. Path. u. Pharm., Schmiedeberg Festschrift, 1908; D. Gerhardt, Zeit. f. klin. Med., vol. lv.

in which case high pressure values, rising to 5 or 6 cm. in terms of a column of water, are formed during the inspiratory phase, additional air being aspirated through the perforation so long as the pressure in the cavity continues to be diminished by the mechanical effects of dyspnea, as explained by Gerhardt. After a few inspirations the pressure in these cases at the height of the inspiration becomes not less than the external atmospheric pressure, and remains positive throughout the rest of the respiratory cycle. The pressure, in other words, oscillates between zero in the inspiration and the positive values named above during expiration, being thus almost constantly positive. This explains the intense dyspnea from which patients afflicted with this type of pneumothorax suffer early in the disease, before any accommodation to the changed condition has taken place. Of course, the fact that the patient is yet able to live and breathe in the presence of an intrapleural pressure oscillating between zero and high positive values is explained only by the compensating increase in the respiratory excursions of the healthy side, in which negative pressure is maintained by increased expansion of the thorax, in spite of the displacement of the mediastinal contents in that direction.

As soon as the perforation accompanying an open pneumothorax is closed, the conditions resemble those existing in the case of a pleural exudate. If fluid be present in addition to the air, the tension pressure must here likewise be distinguished from the hydrostatic pressure of the fluid.

When a fluid effusion appears in an open pneumothorax, the tension pressure may become positive in the inspiratory phase, while the total pressure may be positive throughout the respiratory cycle; however, these conditions, which, of course, exclude all respiratory function on the diseased side, need not exist on the unaffected side of the thorax.

The peculiar conditions of pressure that exist with a recently formed open pneumothorax not only lead to extreme dyspnea, dangerous to life, but must also be considered from the therapeutic standpoint. Unverricht has proposed to treat these patients by establishing communication between the affected side of the chest and the external air, thus converting the condition into a completely open pneumothorax. This proposal seems reasonable at first sight, because the operation does away with any excess of pressure over atmospheric pressure in the pleural cavity. The author, however, has had experience in one such case, which he converted into a completely open pneumothorax by inserting a large drainage-tube through the chest-wall, thus establishing free communication with the external air. The results showed that the circumstances were not at all so simple as imagined by Unverricht, for the condition of the patient became much more serious immediately after this procedure. In fact, the danger of a complete pneumothorax has been recognized generally by the surgeons and is illustrated by their disinclination to operate through the pleural cavity in affections of the esophagus or of the lungs. It was to avoid the danger of causing a pneumothorax that Sauerbruch's positive pressure cabinet and Bauer's negative pressure technic were devised. In the case mentioned above the condition of the patient was again somewhat improved as soon as the the previous state of affairs was reëstablished by shutting off the lumen of the drainage-tube by means of a pinch cock. It was then noticed that the patient could breathe to the best advantage when the communication with the external air was moderately reduced, dyspnea becoming greater as soon as the tube was completely open or shut. Indeed, if the tube was opened to its full extent, the patient seemed to be threatened with immediate death by suffocation. However paradoxic it may seem, yet the expiratory rise of pressure which could be brought on by narrowing the lumen of the tube in the above case, and which normally forms in an open pneumothorax contains a favorable as well as a dangerous element. This is probably explained by the fact that the chief danger of the completely open pneumothorax consists in the tendency of the air inspired by the healthy lung to oscillate between the healthy and the affected side. The unaffected lung, instead of obtaining fresh supplies of air through the trachea, is filled with the air which is partially vitiated by the respiratory exchange taking place in the affected lung, that is, with the "oscillating air," as Brauer has termed it. During expiration the healthy lung pumps part of its own vitiated air into the lung of the affected side, and receives some of it back again with the next inspiration. In addition, it is probable that, by narrowing the communication with the external air to a certain degree, as is done by diminishing the lumen of the tube passed through the perforation, it is possible to hit upon a point which enables the affected lung to participate to a certain extent in the respiratory function. This is the case when the opening in the tube and the valve-like opening in the lung are of such a degree as to result in a certain expansion of the lung in inspiration; while the fact that the air in the pleural cavity does

not immediately escape through the tube in the expiratory phase enables it to exercise a certain pressure upon the lung, and thus help in expelling some of the air from it.

The author's rule, therefore, in case he has to deal with a recent open pneumothorax of the type discussed above, is not to open the pleural cavity completely to the external air, but to puncture the pleural sac by means of a trocar provided with a stop-cock, and then to regulate the entrance of air until the best possible extent of respiratory function is established in the affected lung. So far as the practitioner is concerned, the best instrument for use in emergency is the trocar that usually accompanies Potain's apparatus for the exploratory puncture of the pleura, the lateral opening of the trocar which usually serves for the escape of fluid being previously closed. Another procedure is to introduce a drainage-tube, such as is used in Bulau's method of draining the pleural cavity, and then to regulate the size of the lumen by means of a pinch-cock fastened to the tube, until the most favorable conditions for carrying on the respiration have been established. Instead of using the pinch-cock, the degree of communication with the external air may be regulated by plunging the open end of the tube into a vessel filled with some liquid, the amount of interference with the free communication of the pleural cavity with the atmosphere depending upon the depth to which the tube is plunged into the liquid. In the author's opinion, the best procedure is to use the trocar, which has advantages over the use of the drainage-tube because the instrument may be reintroduced every other day in a new spot where better conditions for effectual respiration may be procured; the drainage-tube, on the other hand, may become loosened by the accumulation of pus about it, and thus be no longer air-tight, so that regulation of the degree of interference with the escape of air is no longer possible. It is impossible, of course, to change the tube from one place to another, because it leaves behind it a widely open perforation which does away with all possibility of affecting the pressure conditions inside the pleural cavity.

The occurrence of sudden death in the presence of pleuritic exudates, aside from the possible hydrostatic pressure upon the heart and the great vessels, especially the veins, caused by the movements of the patient, is thought by Gerhardt to be due to sudden failure of the inspiratory forces. Of course, in cases of very extensive exudate, which may have at first become compensated for by the expansion of the affected side of the thorax, thus mechanically producing negative tension pressure or even a negative total pressure, there may thus suddenly arise a high positive pressure involving the lungs of both the affected and the healthy side, as well as the heart and great vessels. Such pressure, of course, is quite incompatible with the continuance of life.

EXPLORATORY PUNCTURES TO DEMONSTRATE PULMONARY CAVITIES

In addition to physical signs, it is sometimes very desirable, especially for deciding upon an operative procedure, to make use of exploratory punctures, in order to demonstrate pulmonary cavities (tuberculous cavities, bronchiectases, and abscess cavities) and to determine their exact position and size. This naturally succeeds only when the cavities are filled with purulent exudate. It is, therefore, advisable to undertake the puncture at a time when the patient has not expectorated for a long period. Since a small quantity of purulent material may be obtained from a bronchus in bronchial catarrh, it is important to withdraw as large amounts of pus as possible, and to determine by slight movements of the needle whether the latter has penetrated a large cavity, an attempt that will succeed only when the cavities are situated superficially. The contents of pulmonary cavities are usually offensive in odor; for this reason the determination of the odor of the material withdrawn by the puncture, and its identification with the odor of the sputum, are sometimes of considerable significance.

Quite as important a question, in cases where we have determined the existence of a cavity, is whether the cavity is really situated within the lung or is part of an empyema, the indications for operative interference often depending upon such a distinction. The depth from which the pus is withdrawn will often be an important consideration in settling this question. We determine this depth by successive aspirations, pushing the needle little by little back and forth. The characteristics of the pus may also sometimes be employed for determining the position of the accumulation; if it be rather slimy, it is probably partly derived from an intrapulmonary cavity, which is still lined with mucous membrane (bronchiectasis). It may also be noted that the pus of abscess cavities and tuberculous cavities is not

slimy. A mixture of air and pus argues in favor of an intrapulmonary cavity and against an empyema; provided, of course, that the physical signs of a pneumothorax are absent and that we are sure that the syringe is air-tight. The air must also be withdrawn at the same time and from the same depths as the pus, and the amount of the withdrawn pus must prove the existence of a pathologi ccavity. If this be not the case, we must always consider the possibility that the air and purulent material come from a bronchus. The microscopic examination of the purulent fluid furnishes certain data about the nature of the cavity. Such an examination is performed like a sputum examination (elastic fibers, tubercle bacilli, and other bacteria, crystals, etc.). (See p. 703 et seq.) The presence of elastic fibers argues especially against empyema, and in favor of a destructive pulmonary lesion, *i. e.*, cavity formation.

EXPLORATORY PUNCTURE OF THE PERICARDIUM

In exploratory puncture of the pericardium, injury to the heart is best avoided by introducing the cannula almost in the sagittal plane, and directed but slightly toward the median line. The puncture should be made at the left border of the cardiac dulness and to the outer side of the apex-beat, in case the latter be present. The pleura is not considered because no untoward result occurs if it be punctured,

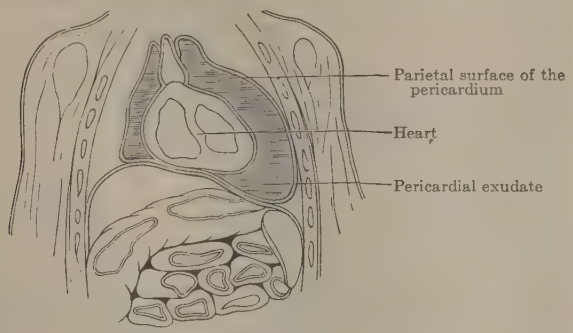


Fig. 362.—Vertical section of a pericardial exudate (Curschmann).

even in case no adhesions have formed between its costal and pericardial surfaces. According to Döbert,[1] however, there are cases in which a puncture in this location gives a negative result, and in which the fluid may be more easily reached through the fourth intercostal space to the right of the sternum. The only cases in which this procedure is applicable are those in which there is a very pronounced and un-

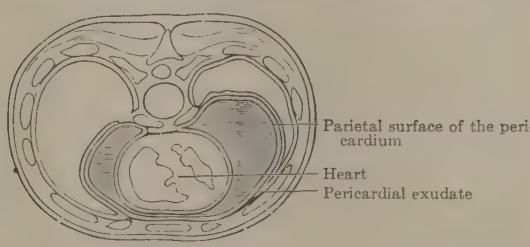


Fig. 363.—Transverse section of a pericardial exudate (Curschmann).

doubted pericardial widening of the cardiac dulness toward the right. In this situation the right ventricle and auricle are uncomfortably close, and their thin walls might easily be injured by the cannula. Paracentesis of the pericardium is much less risky if the sac be punctured from the left side, and this should be looked upon as the procedure of choice. Yet even in this situation no point can be named

[1] Berlin. klin. Woch., 1904, No. 18.

that is suited for paracentesis in all cases. The needle is best introduced in the sagittal direction at the most external limit of the superficial dulness. The choice of the intercostal space should depend upon the height of the diaphragm; in cases normal in this respect the exudate is best reached through the fifth space; if the diaphragm be low, on the other hand, the sixth space should be chosen. The cannula must be cautiously introduced, and the introduction must be suspended at the moment when resistance is no longer encountered or the heart is felt beating against the instrument. Since the danger of injuring a coronary artery or the heart itself (tearing of the thin-walled portions of the heart upon the cannula, Kronecker's "coördination center") is not to be despised and cannot certainly be avoided, the author does not advocate exploratory puncture of the pericardium for purely diagnostic purposes. He believes it should be employed chiefly in those cases of large pericardial exudate in which there is an urgent indication for the removal of the fluid, and then a point must be selected at which the cannula may readily enter the

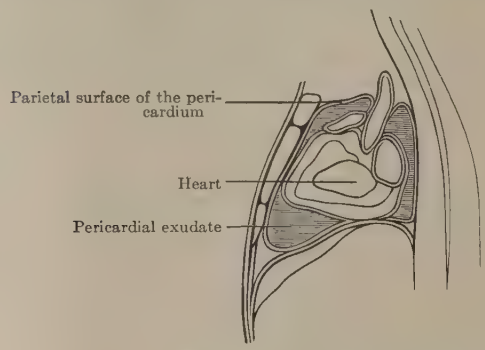


Fig. 364.—Sagittal section of a pericardial exudate (Curschmann).

pericardial cavity. Figs. 362 to 364 show the topographic relations of a large pericardial effusion. The reader should also consult the work of A. Calvert (Johns Hopkins Hospital Bulletin, 1907, vol. xviii, 199), which gives original pictures of cross-sections of cadavers and reproduces the well-known cross-sections obtained by Pirogoff from a cadaver with a pericardial exudate.

EXPLORATORY PUNCTURE OF INTRATHORACIC AND ABDOMINAL TUMORS AND CYSTS

Both in solid tumors and in those with fluid contents exploratory puncture will afford useful data—in the one case by the demonstration of characteristic morphologic tumor elements, and in the other case by the demonstration of fluid which can be accurately examined.

So far as the technical details are concerned, it is almost always a good rule to puncture a tumor only in those places where it lies superficially according to palpation and percussion. It is not wise to puncture through the intestine, although experience has shown that such a puncture with a very fine needle will probably not cause any damage. (See p. 911.)

The diagnostic value of exploratory punctures in *intrathoracic tumors* was well shown in a case of lung tumor at the Bern Clinic. Abundant myelin bodies were found in the fluid withdrawn. They showed in this case even more bizarre shapes than are found in the sputum. (See Fig. 365.) Dr. Zollikoffer proved that these myelin bodies, like those of the sputum, consisted chiefly of protagon (Fig. 276, *g*). The microscopic examination of the tumor showed that these bodies were situated exclusively in the remaining bronchi and alveoli. Their large amount should perhaps be attributed to the stagnation of the secretion associated with the tumor formation. Zollikoffer obtained similar results in studying anatomic preparations of pneumonia and tuberculosis. The appearance is, therefore, not pathognomonic of pulmonary tumors, although in none of the last-mentioned cases was there such an abundance of the myelin bodies as in the pulmonary tumors. The author considers that their presence in the fluid withdrawn by puncture shows surely that the needle

has entered the lung, which is significant in diagnosing the site of intrathoracic tumors, and in distinguishing pleural thickenings from pulmonary consolidations and pulmonary tumors.

Only very fine needles should be employed to puncture cystic abdominal tumors, because, if no adhesions be formed, the fluid may trickle into the peritoneal cavity, and, if infectious, produce serious consequences.

To prove that a cystic tumor is the gall-bladder, it is necessary to determine constituents of the bile in the fluid withdrawn (the bile-tinge to the color, the chemical determination of biliary pigment (p. 575 et seq.), the microscopic demonstration of cholesterin crystals (Fig. 278, *b*). But it must be emphasized that an occluded gall-bladder frequently contains no biliary constituents, cholesterin persisting the longest of any of them. If the aspirating needle strike against hard masses, gall-stones would be strongly suggested.

In the fluid aspirated from echinococcus cysts the microscopic demonstration of *echinococcus scolices*, daughter cysts, and remnants of the laminated membranes (see Fig. 271) is of diagnostic importance. (See the plates in Küchenmeister and Zürn's Die Parasiten des Menschen, 2d ed., Pl. III.) In favorable cases we can sometimes obtain from the fluid in multilocular cysts both scolices and hooks, although, on account of the small size of the bladders, the fluid can be obtained only in traces. However, in this case we should not necessarily expect a positive result, because the majority of the cysts in multilocular type are sterile. Provided the

Fig. 365.—Myelin kernels (protagon) obtained by exploratory puncture from a tumor of the lung.

cortex or investing membrane is not inflamed, the echinococcus fluid is chemically characterized by the absence of proteid content and the presence of succinic acid. (For demonstration see below.)

The thickness of the fluid, *i. e.*, its viscidity—is characteristic of *ovarian cysts* as contrasted with parovarian cysts. Oftentimes this cannot be demonstrated in the fluid withdrawn with a very fine needle; in such cases the chemical demonstration of paralbumin proteid is in itself sufficiently characteristic.

The presence of pancreatic ferment in the fluid withdrawn is suggestive of a *pancreatic cyst*. (See below.) In this connection H. Zeehuisen[1] came to the following conclusions: A positive test for trypsin in the fluid supports the diagnosis of a pancreatic cyst very decidedly, as does the demonstration of a fat-splitting ferment. Negative findings in both instances do not, however, argue with certainty against pancreatic cysts. Diastatic action is useless for the diagnosis, as all sorts of fluids withdrawn possess this peculiarity. The occurrence of tyrosin and leucin crystals in pancreatic cysts is of diagnostic interest (Figs. 278, *c*, 240 and 241).

Hydronephroses and other cysts which are connected with the urinary tract are oftentimes characterized by a considerable urea content.[2] (See below.) However, if the cyst has been shut off for any length of time, urea may be absent. Other fluids of the body, such as blood or serous exudates, contain but little urea except in cases of uremia.

[1] Centralbl. f. inn. Med., 1896, vol. xl, p. 1017.

[2] Traces of urea also occur in exudates and transudates.

Demonstration of Succinic Acid in Echinococcus Fluid.—Hoppe-Seyler[1] describes a method of demonstrating succinic acid in the blood, also applicable to echinococcus fluid. The method is as follows: After the fluid has been carefully acidified with hydrochloric acid, it is freed from albumin by boiling. This is necessary only when the fluid comes from inflamed echinococcus sacs, because ordinarily echinococcus fluid is free from albumin. The clear filtrate is neutralized as exactly as possible with caustic potash, concentrated over a water-bath until it is somewhat thickened, completely precipitated with absolute alcohol, and filtered after cooling (alkaline salts of succinic acid are insoluble in alcohol). The precipitate dissolved in water, filtered, and evaporated may show crystals of alkaline salts of succinic acid. The succinic acid may be dissolved out of the concentrated aqueous solution by shaking the latter with a mixture of equal parts of alcohol and ether acidified with hydrochloric acid, and pure crystals may be obtained by evaporating the filtrate from this solution. Salkowski[2] mentions the following peculiarities of succinic acid for the purpose of identification: It forms four-sided needles, its melting-point is 182° C., it is readily soluble in water, much less so in alcohol, and difficultly soluble in ether. If heated in an ignition tube, the acid melts and sublimes, being partly changed to anhydrous succinic acid. When heated on platinum, the acid volatilizes and forms irritating vapors. If neutral lead acetate be added to the aqueous solution, lead succinate, a heavy crystalline precipitate, appears.

Demonstration of Paralbumin (Pseudomucin in Ovarian Cysts).—Salkowski gives the following rules: 1. A few drops of alcoholic solution of rosolic acid are added to a small quantity (about 25 cc.) of the fluid; the mixture is heated to boiling, and decinormal sulphuric acid is added drop by drop until a yellowish tinge indicates that the reaction of the fluid is acid. The solution is again heated to boiling and filtered. If paralbumin be present, the filtrate is cloudy. 2. The same quantity of the cyst fluid is precipitated with three times its volume of 95 per cent. alcohol and filtered. The precipitate is washed several times with alcohol, dried between sheets of filter-paper, and then shaken up in a mixture of one volume of hydrochloric acid and three volumes of water. The tube is then heated over a wire net to boiling, allowed to cool, and Trommer's test (p. 587) performed with a portion of unfiltered fluid. After boiling, a specimen is cooled off by placing the test-tube in water. Should paralbumin or mucin be present, a precipitate of red copper oxid will form. In differentiating paralbumin (pseudomucin) from mucin, it should be remembered that the former cannot be precipitated from the cyst fluid by means of the acetic acid.

Salkowski's Test for Urea in Cysts of the Urinary Tract.—One hundred cc. of the fluid are exactly neutralized with acetic acid and then poured into 400 cc. of 95 per cent. or absolute alcohol. After it has been shaken and stirred and has stood for twenty-four hours, it is filtered, the coagulum is washed off with alcohol, and the extract evaporated over a low flame. The residue is treated several times with absolute alcohol, and the extract evaporated to dryness. A few drops of nitric acid are added to the residue, after it has cooled off, and it is then allowed to stand in a cool place for twenty-four hours. As a general thing, the nitric acid produces only a cloudiness at first, due to the fatty acids derived from the soaps which are almost always present. Little by little nitrate of urea is thrown down as a crystalline precipitate. This is characterized by the shape of the crystal (Fig. 13), and also by the fact that when the water is drawn off with filter-paper, and the crystal heated, it decomposes energetically or undergoes sudden combustion. No residue may be left, and if present, it being in the melted state, is difficult to see. Should a residue once found give an alkaline reaction when a drop of water is added to it, sodium nitrate is present, in which case the sudden combustion does not signify the presence of urea. Provided the quantity of nitrate of urea is sufficient, it may be identified by the following reactions:

1. Nitrous acid decomposes urea or urea nitrate into nitrogen and carbon dioxid with ebullition of gas.
2. Potassium bromid does the same (p. 630).
3. If urea or urea nitrate be boiled with NaOH or KOH, ammonia is liberated.
4. A neutral (or nearly neutral) solution of mercuric nitrate causes a precipitate even in very dilute solutions of urea or urea nitrate.
5. If urea or urea nitrate be decomposed with furfurol and concentrated HCl, a purple color is developed after a few minutes.

[1] Handbuch der physiologisch-pathologisch-chemischen Analyse, sixth ed., 1893, p. 52.

[2] Practicum d. physiol. u. pathol. Chemie, second ed., 1900.

Demonstration of Pancreatic Ferments in Pancreatic Cysts.—For the demonstration of the tryptic, diastatic, and fat-splitting actions of fluid obtained by puncture see pp. 509 and 513.

PUNCTURE OF THE SPLEEN

Puncture of the spleen, such as is recommended in typhoid in order to demonstrate typhoid bacilli microscopically in the material obtained and by means of culture, is not without danger. The small wound in the spleen in itself is of no particular importance, but the capsule may be considerably torn by the respiratory excursions, as has been shown repeatedly at autopsy. This has often led to severe hemorrhage and symptoms of peritonitis. The author warns against puncture of the spleen, especially since we have at the present time in Widal's serum test a method much more simple and far less dangerous. In any case, care should be taken to perform the puncture rapidly and to see that the patient does not breathe during the act. [Puncture of the spleen in obscure cases of estivo-autumnal malaria is still recommended by some writers.—Ed.]

EXPLORATORY PUNCTURE IN APPENDICITIS

This method in suitable cases is devoid of danger and may be of practical value. It is self-evident that it cannot be applied in cases of diffuse resistance, especially when this is deep and when intestines intervene. There is little chance in these cases of obtaining pus, so that the procedure would be useless, to say the least, if not dangerous. When, however, there is a well-defined tumor over which the percussion-note is dull, an exploratory puncture may be performed without danger. Under these conditions one is sure to pass through already infected tissue, so that the risk of infection is unimportant. One may in this way favor external rupture of an abscess, as the author has personally observed. It may, however, happen, even in cases where the percussion-note is dull over a tumor, that the needle passes through compressed intestines lying between the abdominal wall and the tumor mass. But this does no great harm, as is shown by the cases of puncture performed for therapeutic reasons in meteorism. The author would not, however, have it understood that he recommends exploratory puncture in appendicitis as a necessary and desirable routine measure for determining suppuration. On the contrary, he considers that the procedure is unnecessary for one of experience. He believes that the method has a didactic value chiefly for those physicians who are not familiar with the nature of appendicitis, and who do not believe that all cases of appendicitis are of inflammatory nature. It may also serve to show that quite extensive abscesses may be present in very innocent-appearing cases. Besides this, exploratory puncture may be of a certain amount of value in demonstrating suppuration to people who otherwise refuse operation. The negative result, of course, proves nothing. [It is difficult to understand the author's objections to a rapid exploratory laparotomy for such a purpose.—Ed.]

LUMBAR PUNCTURE

Lumbar puncture attained diagnostic importance for the first time in the hands of Quincke. This writer showed that it is very easy to enter the spinal canal and the subdural space by means of an aspirating needle introduced between the vertebral arches. Fig. 367 represents the arrangement of the lumbar vertebræ in an adult; Fig. 366, that in a child twelve years of age, and shows that the interval indicated by the shaded area is quite sufficient for this procedure. The spinal cord reaches only to the second lumbar vertebra,[1] so that it escapes injury. (See Figs. 366 and 367.) There is also little danger of injuring the cauda equina, because the fibers are sufficiently movable to escape the cannula, and injury to a few fibers would not be productive of any serious trouble. The technic is as follows: The patient is placed on his side and the body bent forward as much as possible, so as to increase the distance between the arches. It is not well to try lumbar puncture with the patient sitting up—at least when performed for therapeutic reasons—as certain disadvantages have been observed due to the change of pressure. Quincke recommended that the puncture be performed between the second and third or third and fourth lumbar vertebræ.

[1] According to Quincke, the cord reaches to the third lumbar vertebra in children under one year.

Subsequent experience has shown that the space between the fifth lumbar vertebra and the sacrum serves just as well and may even be preferable, as the morphologic constituents of the cerebrospinal fluid, such as pus-cells, blood, tubercle bacilli, and trypanosomes, tend to gravitate toward the lowest portion of the dural sac, and might escape observation should the puncture be performed higher. This was shown in a case punctured between the second and third vertebræ, in which the fluid ran clear at first, becoming cloudy later. For the purpose of avoiding error, it is well to count the vertebræ not only from the seventh cervical spine down, but from the sacrum up. It should be remembered that the spines of the lumbar vertebræ are wider and more distinctly separated from each other than those of the dorsal vertebræ; the spine of the twelfth dorsal vertebra, however, resembles the lumbar vertebræ very closely in this respect. It should also be noted that the twelfth dorsal vertebra is marked by the twelfth rib, which starts on the level with its upper border, while the fourth lumbar vertebra lies on the level with the highest point of the crest of the ilium. The needle, to which an aspirating syringe is attached, is introduced under the usual aseptic precautions (see p. 912) in the space chosen, and, according to Quincke, a few millimeters from the median line, so as to avoid the dense ligamentum interspinosum. The point of the needle, however, is directed toward the median line. According to Quincke, the distance to the dural sac in a child two years of age is about 2 cm., and in an adult, 4 to 6 cm. It is just as well

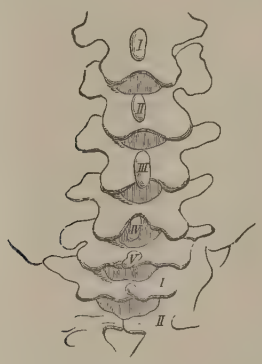


Fig. 366.—Lumbar vertebræ of twelve-year-old child (Quincke).

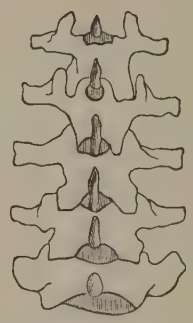


Fig. 367.—Lumbar vertebræ of an adult with sharply inclined spinous processes closing in the intervertebral spaces.

to introduce the needle in the median line, and it would appear to the author that this procedure is somewhat easier. It should be remembered that in a child the spinal processes are short and are directed horizontally, whereas in an adult they are longer and are directed somewhat downward (Figs. 366 and 367). It therefore follows that in children the needle may be introduced midway between the spinous processes, whereas in adults it is best to keep close to the lower margin of the upper process. If the puncture be made in the middle line then, the needle should be introduced in the middle between two spines. In the case of children the needle should be directed straight forward; in adults it is best to push it somewhat upward, corresponding to the anatomic relations of the vertebral spines.

Lumbar puncture is of diagnostic importance in two ways: It enables one, first, to determine the pressure of the cerebrospinal fluid; and, secondly, to determine its peculiarities. It is self-evident that the pressure of the cerebrospinal fluid is immediately influenced by removal of a portion of it, so that tests to determine pressure should be performed before drawing off any of the fluid. An approximate idea of the pressure may be obtained by allowing the fluid to squirt out through the needle after removing the aspirating syringe. If the pressure be low, the fluid appears drop by drop; if higher, the drops come faster; and if extreme, the fluid may escape in a stream. If the pressure, however, is to be measured accurately, the above experiment should not be performed. The simplest way to measure the pressure is to detach the syringe from the needle and to attach to it instead a

very narrow rubber tube (not wider than 1 or 2 mm.), about 30 to 50 cm. long. This change is done quickly, so as to avoid any loss of the fluid. The open end of the tube is now raised, care being taken that it is not kinked at any place, until the flow of the cerebrospinal fluid just stops; the vertical distance between the tip of the needle in the spinal canal and the mouth of the tube at this point gives a direct measure of the pressure in centimeters or millimeters of water. As any careless manipulation by the operator or vigorous breathing of the patient may lead to aspiration of the fluid back from the tube into the spinal canal, care should be taken to have the tube as well as the needle boiled before being used in this connection. To facilitate this method of measuring pressure the author has devised a metal connection the rounded end of which is slipped within the tube, while the other cone-shaped end is inserted into the butt of the needle. This metal piece is attached to the rubber tube before the puncture is made, so that only a few seconds are spent in attaching it to the needle; almost no fluid is lost, this being important not only to insure correct measurement of the pressure under which the fluid escapes, but likewise to diminish the danger of spreading the infection if the case prove to be one of epidemic meningitis. The use of a specially constructed manometer is obviated by this simple method, which is recommended by Quincke as well. If the tube prove to be too short in any given case, it can easily be lengthened by attaching a second tube, which, of course, should also have been boiled and kept ready for any such emergency. The two tubes are joined in the same manner as the first tube and the cannula; the first tube is provided for this purpose with a metal attachment into which a conical metal piece connected with the second tube may be introduced.

As regards the dural pressure under physiologic and pathologic conditions, it may be said that, in the dorsal position, it is 60 to 100 or 150 mm. of water (5 to 7.3 or 11 mm. Hg) under normal conditions, and 200 to 800 mm. of water (15 to 60 mm. Hg) in pathologic conditions, such as meningitis and tumor of the brain. Increase in pressure is likewise characteristic for the long-continued uremic conditions depending probably upon cerebral edema; estimating pressure in these cases is, therefore, of importance from the diagnostic as well as from the therapeutic standpoint. In the interpretation of figures obtained in measuring the pressure of the spinal fluid it must be remembered that increased pressure probably always means a similar state of affairs in the brain, while normal pressure does not necessarily exclude increased pressure in the brain. That the latter statement is correct is well recognized in case of brain tumors, which often lead to the shutting off of the spinal canal from the ventricles by pressing the cerebellum against the edges of the foramen magnum. The author has seen this likewise in cases of epidemic meningitis, the true state of affairs being shown by a cerebral puncture after the spinal canal has been tapped.

After determining the pressure, a specimen of cerebrospinal fluid may be removed for the purpose of examination. It should be remembered that it is not justifiable, in case of simple exploratory puncture, to remove large quantities of the fluid, because of the dangers that supervene when the pressure is reduced below 60 to 80 mm. of water. These dangers have led certain writers to desist entirely from the therapeutic use of lumbar puncture.

The fluid is either withdrawn by aspiration or allowed to trickle out through the tubes of its own accord. This latter procedure has the advantage of withdrawing the fluid gradually, and of allowing one, by holding the tube at a certain level, to prevent the pressure approaching the danger line, *i. e.*, below 80 mm. This may readily be accomplished by holding the open end of the tube 80 mm. above the site of the puncture.

So far as the peculiarities of the fluid are concerned, it will be found that under normal conditions it is colorless, limpid, and of a specific gravity only a little above 1000 (1003). Under such conditions it contains very little albumin (0.2 to 0.5 per cent.), and shows no distinct nucleo-albumin reaction (p. 570). (See p. 941, Nonne-Apelt's test.) An increase of the specific gravity suggests meningitis, although a normal specific gravity may be present in this disease. Lenhartz claims that more than 0.25 per cent. of albumin also suggests meningitis; although the same writer, in exceptional cases of cerebral tumor and apoplexy, has found albumin up to 1.5 to 2.25 per cent. Spontaneous coagulation of the fluid is an important evidence of its inflammatory origin, just as in other puncture fluids. The macroscopic and microscopic appearance of the fluid is of considerable importance. A cloudy fluid indicates inflammation, as does also the presence of numerous white blood-corpuscles on microscopic examination. These are, as a rule, the cause of the cloudiness. On the other hand, the fluid may remain perfectly clear in cases of

inflammation, especially in tuberculosis and even in purulent cerebrospinal meningitis. Marked cloudiness produced by white blood-corpuscles is in favor, generally speaking, of purulent and against tuberculous meningitis. In tuberculous meningitis the cellular elements are, for the most part, lymphocytes, while non-tuberculous and especially meningococcic or pneumococcic inflammation is accompanied by an excess of polynuclear cells. The lymphocyte content of the cerebrospinal fluid has been recently shown to be of some importance in the diagnosis of tabes dorsalis and of progressive paralysis. In these diseases, as well as in other affections of the nervous system, in chronic syphilitic leptomeningitis, and in multiple sclerosis the lymphocytes are usually found to be increased in number, so that the fluid may even appear slightly cloudy. These findings are especially valuable in differentiating initial stages of the above-named affections from neuroses. It should be remembered that, according to Wegelin,[1] the lymphocyte count of the normal cerebrospinal fluid may rise to 50 per cubic millimeter.[2] The degree of cloudiness may, under certain circumstances, serve to distinguish between brain abscess and cerebral meningitis, or to establish a diagnosis of a combination of the two, a point which may be of value in determining the advisability of operative interference. A clear fluid in these cases is against, and a cloudy fluid in favor of, purulent meningitis. In case of meningeal hemorrhage and pachymeningitis hæmorrhagica the fluid has been found blood-stained, a point which may be of diagnostic importance in connection with spontaneous cerebral hemorrhages and softening, although, of course, an intracerebral hemorrhage perforating the ventricle would be liable to cause a hemorrhagic cerebrospinal fluid. Hemorrhagic exudates are also met with in tuberculous meningitis. In tumors of the cord and meninges, one should observe whether the fluid contains tumor-cells, but many cases examined by the author with this in view furnished negative results. Quite recently, however, Stadelman has reported a case of carcinomatous meningitis in which he has succeeded in finding cancer cells in the cerebrospinal fluid (Berlin. klin. Woch., 1908, No. 51).

It is of great importance for the purpose of diagnosis to examine the cerebrospinal fluid for bacteria and other micro-organisms. It is best to prepare dry smears for this purpose, the fluid being previously centrifuged or allowed to settle. (See below, Tubercle Bacilli.) In epidemic cerebrospinal meningitis Weichselbaum's Diplococcus intracellularis will be found. This was formerly confounded with Fränkel's pneumococcus, although there is little resemblance between them,[3] the former being more closely related morphologically and culturally to the staphylococci and still more to the gonococci. The resemblance to the gonococci is so complete that the picture of gonococci on p. 693 may serve to illustrate meningococci as well.

Furthermore, the frequent occurrence of polyarticular inflammation of the joints in cerebral meningitis is in favor of a closer relationship between the meningococci and staphylococci, for there can be no doubt that many cases of polyarticular inflammation are due to coccus infection. The biologic relation of meningococci to gonococci has been demonstrated by Pinto.[4] The meningococcus stands nearest to the Micrococcus catarrhalis, probably being simply a virulent form of this organism. These organisms and the gonococcus have in common their frequent intracellular distribution and their Gram-negative staining reaction, the latter property differentiating them from the common staphylococcus. If simple microscopic examination be negative, culture methods may be used, though it must be remembered that the meningococcus grows only if the spinal fluid be planted as soon as obtained. The organism grows best at incubator temperature on plain agar or, still better, on ascitic agar. Other important excitants of meningitis are pneumococcus, which is often responsible for small epidemics of the affection; staphylococci, streptococci, etc., have been found in other cases. In cases of the African sleeping sickness trypanosomes, with or without streptococci, have been found in the cerebrospinal fluid. In tuberculous meningitis it is quite surprising that tubercle bacilli are found in the puncture fluid in 50 to 75 per cent. of the cases. They are found most easily after allowing the fluid to settle for some time until a coagulum appears, from which a dry preparation is made. (See p. 709.) In cases

[1] Wegelin, Ueber acut verlaufende multiple Sklerose, Deut. Zeit. f. Nervenheilk., 1906, vol. xxxi, p. 313.

[2] In the Lichtheim Clinic the fluid is diluted with an equal volume of 0.5 per cent. acetic acid, and the cells in a drop of the dilution are counted in a counting chamber.

[3] H. Jäger, Zeit. f. Hyg., vol. xix, p. 351. This work contains photographs of the Diplococcus intracellularis.

[4] Jour. de physiol. et path. gén., 1904.

where no coagulum forms the fluid must be centrifuged or allowed to settle for some time, so that the bacteria will sink to the lower layers. Tubercle bacilli are especially easily found if the spinal fluid be mixed with equal parts of alcohol before being centrifuged, the reasons for using this method being the same here as those given in the case of the urine. Should the fluid contain nucleoalbumin (pp. 939 and 941), it is well to precipitate this with acetic acid, then centrifuge, and hunt for the tubercle bacilli in the isolated precipitate. (See Examination of the Sputum according to Ilkewitsch, p. 714.) The author has frequently seen mixed infections with tubercle bacilli and meningococci, so that it is advisable, from the standpoint of prognosis, to seek for tubercle bacilli after meningococci have been demonstrated. The fact that tubercle bacilli are so frequently found in spinal fluid, while their presence in pleural exudate is but rarely demonstrated, shows that they probably multiply in the former liquid; this assumption, as well as the finding of miliary tubercles in the interior of the subarachnoid space, seems to the author of significance in explaining the origin of isolated primary tuberculosis of the meninges.

For Wassermann-Neisser-Bruck's serum reaction in syphilis see p. 863.

EXAMINATION OF THE CEREBROSPINAL FLUID BY THE NONNE-APELT METHOD

Equal parts of the spinal fluid are mixed with an 80 per cent. solution of ammonium sulphate, saturated while hot, then filtered and cooled. The specimen is allowed to stand three minutes. Normal spinal fluid shows no change. In certain cases, at the end of three minutes, more or less turbidity is apparent (globulin and nucleoalbumin). An essential for the reaction is that the fluid contain no blood, the presence of which would simulate a positive reaction. According to Nonne-Apelt's observations, which have been confirmed by others, the action occurs very frequently in luetic affections of the nervous system, as well as in non-luetic affections which exhibit a lymphocytosis in the fluid. In neuroses, on the contrary, there is no reaction. Nonne-Apelt emphasizes the very important therapeutic fact that the reaction is negative in healed syphilitic lesions. He sees in the reaction a subtle differential diagnostic sign for distinguishing between tabes and progressive paralysis, on the one hand, and neuroses, on the other. According to K. Wirth and Schlesinger,[1] the reaction is also positive in cerebral tumors, infectious diseases, multiple sclerosis, and cerebral abscess.

[NOGUCHI'S BUTYRIC ACID TEST FOR SYPHILIS[2]

This reaction depends upon the fact that the globulin fraction of the blood-serum and cerebrospinal fluid is increased in syphilis. The increase is usually associated with the appearance of a syphilitic antibody, but is recognizable earlier than the latter. The method of detecting this increase in globulin is as follows: 0.1 cc. cerebrospinal fluid free from blood is mixed with 0.5 cc. 10 per cent. butyric acid solution in physiologic salt solution and the mixture heated over a Bunsen flame; 0.1 cc. of a normal solution of NaOH is added quickly, and the whole is then boiled for a few seconds. The presence of an increased content of protein is shown by a granular or flocculent precipitate, which gradually settles at the bottom of a clear supernatant fluid. This appears in a few minutes to two hours after the second heating, depending on the amount of globulin present. It occurs regularly in syphilitic and parasyphilitic affections, as well as in meningitis caused by Diplococcus intracellularis, pneumococcus, influenza and tubercle bacilli; diseases which can, as a rule, be readily differentiated from syphilis by other symptoms. Normal cerebrospinal fluid gives a slight opalescence but no precipitate in less than several hours.

A comparison of the results obtained with this test and those of Wassermann's reaction and the cytodiagnostic test is of interest. In a group of cases of hereditary syphilis the butyric acid test was positive in 90 per cent.; the Wassermann reaction in 80 per cent. The butyric acid test was positive in all cases of

[1] See Neurologische Centralbl., 1908; also Zeit. f. Nervenheilk., vol. xxxvi, Nos. 1 and 2. (Bericht der Jahresver. der deutschen Nervenärzte, Heidelberg, 1908.) More recent observations have been made by K. Wirth and Schlesinger, Mitteilungen der Gesellschaft für innere Medicin und Kinderheilkunde in Wien, 1909, No. 1.

[2] Noguchi, Serum Diagnosis of Syphilis, J. B. Lippincott Co., Philadelphia, 1910.

cerebral and spinal syphilis; the Wassermann in only 50 per cent. In general paresis the butyric acid test was positive in 90 per cent., the cytodiagnostic test in 91 per cent., and the Wassermann in 73 per cent. In tabes dorsalis the butyric acid and cytodiagnostic tests were positive in all cases; the Wassermann in 53 per cent. In psychoses, in which syphilis could be excluded or in which no history of syphilis could be obtained, the butyric and cytodiagnostic tests were positive in 2.8 per cent.; the Wassermann (original method) in 13 per cent.—Ed.]

EXPLORATORY PUNCTURES OF THE BRAIN

Exploratory puncture of the brain, through the skull, during life was first recommended by Maas, and the technic was worked out by Schmidt, Payr, Kocher, Sr. and Jr., Neisser, and Pollack. (For details, see the two last-named writers.) Exploratory punctures of the brain serve to estimate the cerebral pressure in meningitis, brain tumor, and hemorrhage, and they may also be used to aspirate, for diagnostic purposes, fluid (cerebrospinal fluid, pus, blood) or solid tissue-particles (tumor tissues). As in lumbar puncture, the diagnostic procedure is often immediately followed by the therapeutic decompression operation.

Cerebral puncture can be performed almost painlessly with novocain, or with the ethyl chlorid spray, without a general anesthetic. A hand-drill, or a drilling machine driven by electricity or with the foot, may be used for the actual boring process. The drill ordinarily used is a chisel-shaped instrument, such as metal workers employ. Neisser and Pollack recommend drills having a diameter of 2⅓ to 2⅔ mm. The author employs a hand-drill, with a handle at the side, and an ordinary bit, 2.5 mm. in diameter, instead of the usual chisel-shaped drilling blades. This bit terminates in a blunt cone, and presents in the longitudinal direction four sharp, screw-shaped edges. It is superior to the chisel previously employed by him, for by reversing, it can be very easily removed from the hole, whereas the ordinary drills are apt to bind. After the example of Middeldorpf and others, the author has had a movable sheath added to the drill, which can be pushed over the blade, and, by means of a screw, so fixed as to regulate the depth of penetration, and at the same time prevent the sudden violent impact of the drill against the dura and the brain, when the resistance ceases after the skull has been perforated. Since the point of the drill is very blunt, the soft parts must first be incised with a sharp, slender knife (cataract knife). This precaution possesses another advantage in preventing the introduction of micro-organisms from the skin by means of the drill.

The technic is as follows: A considerable area of skin around the point chosen for the puncture is shaved, and the point selected is marked with carbolfuchsin. The shaved region is then disinfected in the usual way. The ethyl chlorid spray is used for local anesthesia, and, if desirable, novocain, with an addition of adrenalin (2 per cent. novocain with 0.01 per cent. adrenalin), is injected through the frozen part. An incision having been made down to the bone, the sterile drill is applied perpendicularly to the surface of the bone, and the bone is perforated under light pressure upon the rotating drill. The instant of perforation of the external and internal tables can be easily appreciated. The sheath prevents the drill from entering too far after the bone has been pierced. With a little care injury to the dura can be avoided. The rotation is then reversed and the drill drawn out. It is important to avoid any displacement of the skin, in drilling as well as in removing the drill, so that the perforation may be readily located afterward with an exploratory cannula. After the drill is removed, the skin is cleansed of the accumulated material. In case of hemorrhage it is better to let the blood escape externally than to staunch the flow by closing the orifice, for this might give rise to hematoma. The exploratory puncture is then performed through the orifices, with the syringe described on p. 911. It is advisable to aspirate at first only in the area of the orifice, without going deeper, in order to remove any extradural fluid that may be present. Later on, the dura is perforated by means of the cannula, which is then introduced into the brain, first perpendicularly, then in various oblique directions. Any lateral movement of the cannula must, of course, be avoided, in order to protect the brain. Before puncturing in a new direction, the point of the needle must be withdrawn each time as far as the dura. In order to avoid the blocking of the cannula with brain-substance, Neisser and Pollack recommend that it be armed with a mandrin of fine steel wire, which is removed just before aspirating. As in any other exploratory puncture, it is, of course, necessary to aspirate at different depths. After withdrawing the cannula, the wound is closed with a small piece of

court-plaster, moistened in bichlorid solution; it heals normally by first intention, but Neisser and Pollack point out that the bone wound, which is closed at first only by granulation tissue, remains permeable to the puncture needle for a long time (three months in one instance), a point that may acquire importance should the puncture have to be repeated later on.

Puncture of the lateral ventricles, at the present time the most important procedure for the clinician, was apparently replaceable by Quincke's method of lumbar puncture for all diagnostic and therapeutic purposes, until it was found that in certain cases, especially in tumors of the posterior cranial fossa, the communication between the cerebral and spinal fluids is interfered with, so that reliable conclusions as to the condition of the brain cannot always be based upon the state of the pressure, or the composition of the fluid obtained by lumbar puncture. Moreover, the therapeutic decompression of the brain is not in all cases so readily accomplished by way of the spinal canal as through puncture of the ventricles. The author recently observed a case of epidemic cerebrospinal meningitis, and also one of brain tumor, in which lumbar puncture had not shown an increase of pressure during the life-time of the patient, although the existence of intracranial pressure was demonstrated at the autopsy.

Reliable topographic landmarks are indispensable for the performance of puncture of the ventricles, in order to reach them with absolute certainty, without unduly damaging the surrounding parts. Of course, only the lateral ventricles are adapted to puncture, puncture of the anterior horns being the most advisable, because probably the least damage is incurred by the necessary injury of the frontal lobes. Kocher selects for ventricular puncture a point in front of the precentral sulcus, between the middle and upper frontal convolutions; this spot corresponds to a point on the surface of the skull, 2.5 to 3 cm. to the side of the so-called bregma, *i. e.*, the junction between the sagittal and coronary sutures. The motor centers are thus avoided, the normal anterior horn of the lateral ventricle being reached at a depth of 5 to 6 cm. The needle is introduced in the direction of the longitudinal axis of the body.

As it is often impossible to feel the bregma, Neisser and Pollack advise that a line be drawn from a point immediately below the nose to the external end of the bony auditory meatus, and a perpendicular be erected on this line, starting at the auditory meatus; this perpendicular should intersect the median sagittal line of the skull at the bregma. Cerebral puncture is fairly free from danger, according to the reported observations, in those cases at least in which it is performed at this typical site. Arterial hemorrhage or profuse venous bleeding may be avoided if the above site for puncture be chosen.

In the exploratory ventricular punctures the same methods of examination are used as in lumbar puncture. The estimation of the cerebral pressure is naturally of the greatest interest, but, unfortunately, very little is known concerning the normal pressure of the cerebral fluid, this weighty question being left undiscussed even in the comprehensive article of Neisser and Pollack. According to Naunyn and Falkenheim, the ventricular pressure in the dog varies normally between 30 and 140 mm. of water. We do not know to what extent these figures are applicable to man. It is known, however, that in pathologic intracranial pressure in man the pressure of the ventricular fluid may approach that of the blood.

Localization of the Individual Lobes and Regions of the Brain (according to Neisser and Pollack).—This refers to brain punctures not only for the purpose of entering the ventricles and evacuating ventricular fluid, but also for exploring the brain substance itself, or the subdural space, at various points. (See Fig. 368.)

Frontal Lobe.—The two points utilized for puncture by Neisser and Pollack are situated in a line drawn backward through the middle of the supra-orbital ridge, parallel to the median line. The first of these points (F_1, lower frontal point) lies on this line at a distance of 4 cm. from the superciliary margin; the second point (F_2, upper frontal portion) lies at the same distance higher up.

Cerebellum.—The cerebellum is generally punctured by Neisser and Pollack in the middle of the line connecting the external occipital protuberance and the tip of the mastoid process (point K). The needle strikes the center of the corresponding cerebellar hemisphere (at the lower aspect of the lobus gracilis, emerging above approximately in the middle of the lobulus quandrangularis). In drilling the hole, the instrument must be held perpendicularly to the outer table, according to Neisser and Pollack, and the handle of the instrument must be depressed considerably toward the neck, because the bone surface is by no means parallel to the direction of the skin surface.

Central Convolutions.—In the first place, it is necessary to determine the position of the precentral sulcus (Kocher). For this purpose the sagittal meridian is drawn from the external occipital protuberance to the glabella, and the equatorial or base line as the shortest line between the external occipital protuberance and the root of the nose. The sagittal meridian is then bisected, and a very short line is drawn downward and forward from its midpoint, forming an angle of 60 degrees with the sagittal meridian. This is the so-called *anterior oblique meridian.* Kocher showed that this corresponds to the precentral sulcus almost in its entire length, only the uppermost portion overlying into the central convolution. (See Fig. 368.) When this anterior oblique meridian is divided into three equal parts, the beginning

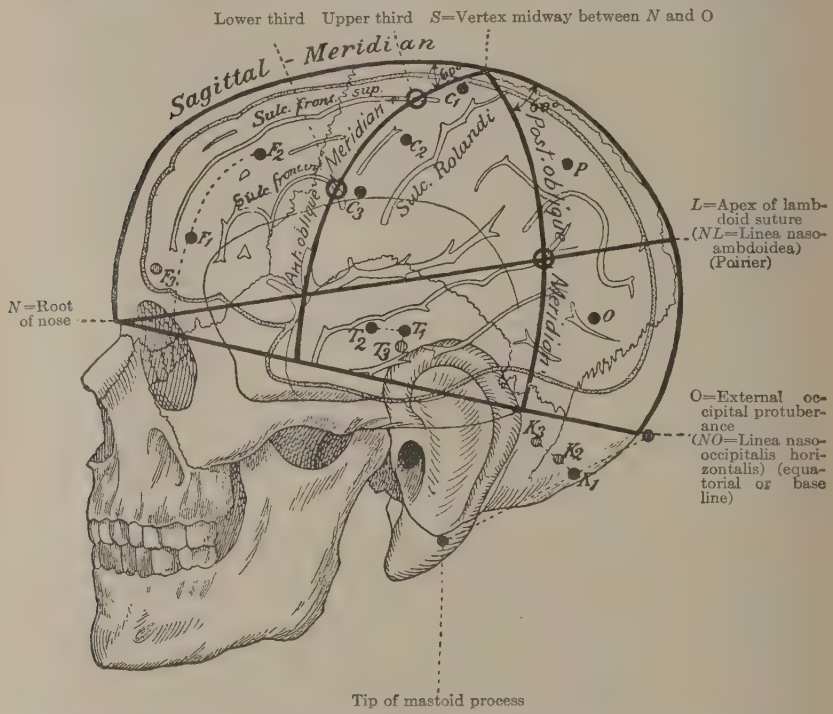


Fig. 368.—Diagram of craniocerebral topography (Poirier-Kocher). Puncture-points, according to Neisser and Pollack. (Mitteilungen aus den Grenzgebeiten der Medizin und Chirurgie, 1904, vol. xiii.)

▬ Lines corresponding to Kocher's craniometric points.

◍ Abscess points. } According to Neisser and Pollack.

● Points for exploratory puncture of the individual lobes. } According to Neisser and Pollack.

of the sulcus frontalis superior corresponds, according to Kocher, to its upper third, and the beginning of the sulcus frontalis inferior to its lower third. The course of the middle meningeal artery corresponds to the course of the precentral sulcus, the main anterior branch to the parietosphenoidal sinus. To avoid hemorrhage, therefore, puncture is advisable only in that portion of the central convolution area lying above the lower third of the anterior oblique meridian; Neisser and Pollack recommend keeping from ½ to 1 cm. behind the course of the middle meningeal artery, mapped out as above. The leg-center (C_1) is then reached above the upper third of the oblique meridian; the arm-center (C_2), between the upper and lower third; and the facial center (C_3), at the lower third.

Temporal Lobe.—The following points are suggested by Neisser and Pollack: The first (T_1) lies 1 to 1.5 cm. directly above the upper insertion of the concha (on a line perpendicular to an imaginary horizontal line passing through the infra-orbital ridge and the highest point of the external auditory meatus). The second point (T_2) lies 1.5 cm. further toward the front, in a direction parallel to the imaginary horizontal line.

Parietal and Occipital Lobes.—The posterior oblique meridian is drawn (see Fig. 368) from the middle of the sagittal meridian backward and downward at an angle of 60 degrees; then the nasolambdoidal line is drawn from the apex of the lambdoid suture, which is usually plainly palpable, to the root of the nose. The posterior oblique meridian thus bounds the supramarginal gyrus anteriorly, and the angular gyra posteriorly, above the nasolambdoidal line, whereas below this line it separates the temporal lobe from the occipital lobe. The boundary line between the occipital and parietal lobes is not clearly defined, and the reader is referred to the illustration for further details. According to Neisser and Pollack, the vascular relations permit safe punctures in these regions.

Points of Puncture for Typical Abscesses and Hemorrhages.—Besides these general rules for punctures in the area of definite parts of the brain,—which are selected especially with regard to the normal topography, and in order to avoid large blood-vessels,—certain special points are designated as affording the best prospects for reaching typical sites of brain abscesses and extrameningeal extravasations by means of puncture. In this connection the following should be mentioned:

Abscess of the Temporosphenoidal Lobe.—The puncture is best made 0.5 to 0.75 cm. vertically above the insertion of the concha (vertically is here used in the sense of the terminology adopted above), perpendicularly to a line drawn through the highest point of the auditory meatus and the root of the nose (T_3, Fig. 368).

Cerebellar Abscess.—Small incipient cerebellar abscesses, which are usually situated in the sigmoid fossa, may be reached by puncture half-way between two points, one of which, K_1 (see Fig. 368), lies half-way between the external occipital protuberance and the tip of the mastoid process; the other, K_2, corresponding to the posterior upper angle of the mastoid process (the highest palpable point of its posterior margin). The point K_2 (Fig. 368), which is ascertained in this way, lies in the flexure formed by the sigmoid sinus, but at a sufficient distance from the sinus itself. The puncture must here be directed as nearly perpendicularly as possible to the outer table, which in this locality does not lie parallel with the surface of the skin. The point K_1 is also a good place for the puncture of *large* abscesses.

Rhinogenous Brain Abscesses.—The lower frontal point F_1 and the point F_3 (see Fig. 368) are points of election for the puncture of these abscesses.

Localization of Hemorrhages.—Kroenlein's two trephining points (see Corning, Topog. Anat., 1907) are the landmarks used in searching for extradural hemorrhages. They are situated on a horizontal line drawn backward from the supra-orbital ridge; the anterior 3 to 4 cm. behind the malar process of the frontal bone, the posterior at the point of intersection of this line with a vertical line through the posterior margin of the mastoid process. (The horizontal direction is here again supplied by the connecting line of the infra-orbital margin with the highest point of the external auditory meatus.) In view of the fact that Kroenlein's points correspond as closely as possible to the position of the anterior and posterior branch of the middle meningeal artery, it is recommended that the punctures be made a trifle posterior to these points, so as to avoid the accidental injuring of the artery.

HARPOONING

To obtain small pieces of deep-seated tissue for histologic examination harpoon-like instruments have been introduced through a cannula and then projected beyond the protecting sheath, to be subsequently drawn back into the cannula with a portion of the tissue desired. As a rule, harpooning is unnecessary, as it is usually possible to obtain sufficient tissue for an examination by using the ordinary aspirator in the manner explained on p. 913. At any rate, the harpoon will be used only in cases where the aspiration fails or where larger particles are desired for the purpose of making microscopic sections. These harpoons may be obtained from an instrument-maker, or they may be improvised by cutting a notch in the stilet of an ordinary trocar. Care should be taken not to have the notch in the stilet so deep that there is danger of the bob breaking off. Harpooning is a much more severe procedure than the exploratory puncture, because, for safety, it is essential that the

harpoon be of a certain thickness. Generally speaking, harpooning has been justly given up.

Von Plesch[1] has recently devised a new instrument for obtaining pieces of tissue for examination without causing the crushing injury resulting from harpooning. It is claimed for this instrument that even a bit of bone-marrow can be removed from a living patient. The advisability of so heroic a method of diagnosis is, however, open to doubt.

EXAMINATION OF THE NERVOUS SYSTEM

Although the technical aids to the examination of the nervous system are usually simple and require but brief notice, it is more important in this department of internal medicine than in any other to conduct the examination in accordance with a definite logical plan. The complex functions of the nervous system make such a plan essential in order that no symptoms may be overlooked, and that the symptoms may be so grouped as to suggest the diagnosis. Such systematic procedure takes time; but it is quite simple and, in fact, often easier than in other forms of disease, since the examiner needs less technical skill. The reason why the beginner finds the diagnosis of nervous diseases so difficult is because he is not familiar with those anatomic and physiologic facts which are absolutely essential for the accurate interpretation of clinical cases.

GENERAL PART

I. PSYCHIC EXAMINATION

The clinician now and then observes in his patient mental disturbances which belong exclusively to the domain of psychiatry. For a comprehensive method of examination in such a case it is advisable to consult text-books upon that subject. In this volume we shall describe those psychic disturbances only which occur so frequently in clinical medicine as to be typical. These include the various grades of depression or irritative disorders of consciousness, delirium, and disturbances of intelligence and memory. Language, which lies on the border between physical and psychic function, will be considered in a separate chapter.

DEPRESSED DISTURBANCES OF CONSCIOUSNESS

The term *somnolence* (sleepiness or hebetude) is applied to the mildest grade of a depressive disturbance of consciousness. This merges imperceptibly into lethargy or stupor, and finally into *coma*, or absolute loss of consciousness.

These depressive disturbances of consciousness are observed not only in brain diseases, but also in all sorts of general affections: 1. In any lethal illness, a short time before death. 2. At the height of infectious febrile diseases, though such diseases rarely produce complete loss of consciousness. 3. In uremia, and then they are generally accompanied by convulsions. 4. In diabetic coma. The deep, often hurried breathing, the so-called air-hunger (Kussmaul), with gradual loss of consciousness, which generally becomes complete, is very characteristic.

[1] Deut. med. Woch., 1906, p. 721, No. 18.

(See p. 99.) 5. In cases of poisoning, especially with alcohol, morphin, chloroform, chloral hydrate, coal-gas. 6. In epileptic attacks. 7. In many hysteric attacks. 8. In focal lesions of the brain of sudden onset, hemorrhage, softening (shock, stroke), in traumatic cerebral lesions (laceration, concussion), in the different varieties of meningitis, and in the later stages of brain tumors.

The disturbance of consciousness noted in *hysteria* is distinctive. If complete, it is ordinarily called *lethargy*. It can be differentiated from the comatose conditions observed in severe brain diseases (apoplexy, uremia, etc.) because it simulates normal sleep so perfectly. This peculiarity (*i. e.*, similarity to sleep) of the hysteric lethargy, enables the experienced observer to differentiate it at a glance from the severer form of disturbed consciousness. It is due essentially to an interruption only of cortical function, so that the phenomena accompanying other forms of coma, which depend upon infracortical disturbances, such as stertorous or interrupted breathing, cyanosis, recognized as grave even by the laity, are lacking. The hysteric condition of lethargy differs from normal sleep in that the former arises and persists under conditions which would prevent or interrupt the latter. Quite a series of transitional forms may occur in the hysteric between lethargy (hysteric unconsciousness) and alert consciousness, *e. g.*, *somnambulism*, in which a person, without any subsequent recollection, may perform all kinds of complicated actions, influenced apparently by no ordinary motives, but by constraining ideas. During the somnambulistic condition the memory seems to be cognizant of what has occurred in previous attacks, whereas in the interval everything relating to the somnambulistic condition is effaced from consciousness (dual personality). These transitions between absent and present, or, better, between waking and sleeping consciousness, may be produced artificially in certain persons by hypnotic, *i. e.*, suggestive, influence, and are, therefore, called *hypnotic conditions*. Wundt regards them as limitations of consciousness; in other words, certain anatomic substrata in the brain are sleeping, *i. e.*, inhibited, whereas other areas functionate much more actively, and in consequence of their isolation, oftentimes in peculiar fashion. A motor phenomenon frequently connected with hysteric disturbances of consciousness is the so-called *catalepsy* or *cataleptic muscular rigidity* described upon p. 961. Such hysteric (hypnotic) conditions associated with cataleptic rigidity are ordinarily designated as *catalepsy*, although the latter expression should really be limited to the condition of the motor system, and not include that of the consciousness.

IRRITATIVE DISTURBANCES OF CONSCIOUSNESS

Delirium is practically the only one of these irritative disturbances which concerns the clinician. It means a dream-like, cloudy state of consciousness, generally associated with hallucinations in which the intellectual capacity is altered in a morbid, irritative way. It does not preclude a depressive condition in other fields of consciousness, and so delirious patients may at the same time exhibit stupor. Delirium is frequently accompanied by *hallucinations* and *illusions*. We distinguish a *noisy* from a *quiet delirium*. The highest grade of the former is the so-called *maniacal delirium*. In *muttering delirium* the patient lies quietly in bed and mutters softly to himself. Delirium may be observed in any severe general condition; it is especially frequent in fever, and then it nearly always denotes a severe sickness. But we should remember that children become delirious more readily than adults, just as in fever their temperatures run higher; and that the weak-minded become delirious very easily. Many acute brain diseases manifest active delirium.

The irritative disturbances of consciousness which accompany the depression in hysteria and which occur especially in the so-called "hysteria major" as a variety of delirium, should be attributed partly to the lack of inhibition, as a result of depressive states of other fields of consciousness.

The *delirium of alcoholism* (*delirium tremens*) is very characteristic. It is, for the most part, a very noisy, maniacal form, and is almost always associated with hallucinations. The patient sees black forms, mice, bugs, snakes, wires running through the air, a policeman, etc. These appearances have been attributed to the presence of scotomata in the visual field; but if this explanation were correct, the condition would be one of illusions, or of errors in sight, not of real hallucinations. The typical tremor which almost always accompanies delirium tremens may decide the diagnosis.

Most cases of quiet delirium which are noticed in patients seriously ill, and which are accompanied by *carphologia* or *floccillation*, render the prognosis rather grave. The patient lies completely oblivious of his environment, continually picking at the bed-clothes, or making motions with his fingers as if he would pick off flakes or scales. Carphologia, a symptom which generally precedes death only by a short time, probably depends upon hallucinations.

DISTURBANCES OF THE INTELLIGENCE

These may be independent of any of the disturbances of consciousness, although they are frequently associated with them. The patient's history or a previous acquaintance with him is all there is to aid the

Fig. 369.—Cretinismus (Dr. F. C. Shattuck, Massachusetts General Hospital).

Fig. 370.—Cretinismus. Same case as Fig. 369 after treatment (Dr. F. C. Shattuck, Massachusetts General Hospital).

physician in appreciating the milder grade of disturbances of the intelligence. On the contrary, the severer grade (*stupidity*) and the highest grade (*imbecility*) are evident enough from the facial expression and deportment of the patient.

Any of the incurable maladies may be accompanied by the milder disturbances of the intelligence, *e. g.*, *heart disease, nephritis*. Severe disturbances, *i. e.*, marked *stupidity* or *imbecility*, on the contrary, point with much probability to disease of the brain, and, if we except actual psychoses, they point to *brain tumor, paralytic dementia, multiple sclerosis*, or the after-effects of acute focal lesions of the brain, such as *hemorrhage and softening*. In other cases *imbecility* is the expression of a congenital or early acquired cerebral anomaly (*idiocy* or *cretinism*). The disturbance of intelligence which is observed in *myxedema*, spontaneous or operative (such as after removal of a goiter), deserves special mention. This condition is either very closely related to or identical with cretinism. Such patients exhibit sometimes mild mental disturbance, such as slowness of thought; sometimes, however, a much more serious trouble, bordering on real imbecility.

DISTURBANCES OF MEMORY

Memory is frequently appreciably impaired in old but otherwise quite healthy persons. In other cases it may be affected under the same conditions as the intelligence. In fact, after acute lesions of the brain (hemorrhage and softening) a weakness or even sometimes a complete loss of the memory is very often noticed, and frequently it persists, although the intelligence is not necessarily affected. The so-called traumatic neuroses are very often accompanied by a failing memory.

II. EXAMINATION OF MOTILITY

1. PARALYSIS

To demonstrate paralysis the examiner requests the patient to perform voluntary motions, either without or against resistance. If paralysis of the muscles exists, such a movement is either not performed at all (complete paralysis) or more slowly and less completely than normally (*incomplete paralysis, paresis, motor weakness*). We easily recognize severe paralysis or even motor weakness in this way. In many instances the posture of the body at rest is in itself so distinctive that we need no attempt at motion to appreciate the complete loss of power. For example, a paralysis of the eye muscles is often evident from the abnormal position of the eyeball; facial paralysis, from the asymmetry of the face; paralysis of the arm, from the dropping and dangling of the arm; peroneal paralysis, from the drooping of the tip of the foot (equinovarus); a musculospisal paralysis, from the *wrist-drop;* an ulnar paralysis, from the characteristic *claw-like* position of the fingers (extension of the proximal phalanges and flexion of the terminal phalanges); a median-nerve paralysis, from the abduction and extension of the thumb, simulating the ape hand. We must, however, always combine inspection with an attempt to secure voluntary movements, since to make a diagnosis it is necessary not only to determine a paralysis, but also to localize it exactly, and so we must test separately the functions of the individual muscles and muscle groups. The cranial nerve-supply will be found upon pp. 1039 to 1094; the nerve-supply of the muscles of the remainder of the body upon pp. 1132 to 1136. If the paralysis be unilateral and not very marked, the examination is made easier by comparing the healthy with the affected side. In this way we can demonstrate a mild

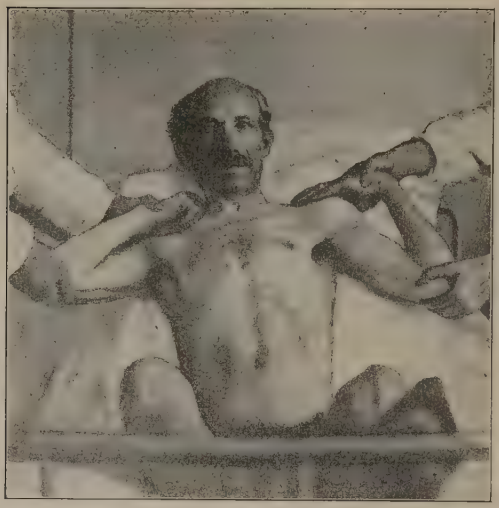


Fig. 371.—Right hemiplegia, organic; excessive flexion of the right forearm upon the arm.

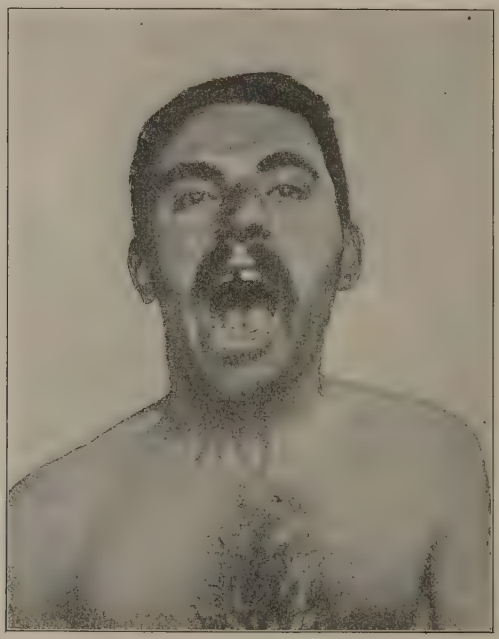


Fig. 372.—Left hemiplegia, organic; sign of the platysma. The paralysis of the platysma upon the left side is evident.

hemiplegia, or, if it be severe, weakness of the trapezius, the respiratory, or abdominal muscles, which otherwise might easily have escaped the

examiner's notice. The rapidity, the force, and the excursion of the movement should all be noted. An excellent method for detecting a very slight one-sided paresis of an arm or a leg is to have the patient raise both extremities as quickly as possible at the same time. The paretic arm or leg will then be plainly seen to lag behind the healthy member, and to fall more quickly from the raised position, even in cases where, in testing the power by movements against resistance, we can scarcely appreciate any abnormality. We can utilize the hand dynamometer to test the strength of the hand.

A mechanical limitation of movement in a joint, or pain incident to its movement, sometimes makes the movement weak, ineffectual, or almost lacking, and so is responsible for an erroneous diagnosis of motor paralysis or paresis. Therefore, before assuming the presence of a motor weakness, we should particularly examine for such a condition of affairs. Of course, patients will have to be believed in regard to the influence of pain upon motility, although they are often very unsatisfactory in their statements. They will acknowledge that they feel pain, but deny that it is responsible for the interference of motion. Frequently they are firmly convinced of the existence of a paralysis until the pain subsides under treatment and permits perfect motion. A sufficiently large dose of morphin administered hypodermically will settle the matter and show that the movement is unconsciously limited by the pain. Such motor weakness is responsible for certain hysteric paralyses where the inhibition of motion outlasts the sensation of pain.

[Babinski has called attention to several aids in differentiating an organic from a hysteric hemiplegia. Two of these are well illustrated in the accompanying cuts (Figs. 371 and 372), and a third in Fig. 378, p. 960, copied from his article.[1]—Ed.]

2. PHENOMENA OF MOTOR IRRITATION

(*a*) Clonic Convulsions or Contractions; Clonic Spasms

By these we mean involuntary muscular contractions repeated in shocks or series, generally with considerable force and rapidity, and contrasted with voluntary contractions badly coördinated. Thus, in spite of the great expense of power, there often results only very slight movement, because antagonistic muscles are working in opposition. An epileptic attack and the typical uremic and eclamptic spasms are types of the clonic convulsion.

Clonic convulsions are never occasioned by peripheral excitation of motor nerves. An accumulating irritative center whose action may be compared to that of a Leyden jar seems to be essential to set off the shock-like explosions. Clonic contractions are practically always occasioned either by a direct or by a reflex irritation of a motor center, whether it be the nuclei or the psychomotor centers of the cortex.

(*b*) Tonic Convulsions; Tonic Spasms or Cramps

By tonic convulsions we understand long-continued rigid contractions of muscles which may change suddenly and lead to prolonged change of position or tension of the muscles implicated. Tonic convulsions may, under some circumstances, be associated with or even transformed into the *clonic* variety. Tetanus is the type of a tonic convulsion. Tonic convulsions originate in nearly all cases from irritation of some

[1] Gaz. des Hôp., 1900, No. 52, p. 521.

center, and generally reflexly from a nucleus, as, for instance, in tetanus, strychnin tetanus, tetany, and the rigidity of the neck and back in meningitis. The well-known cramp of the gastrocnemius which is

Fig. 373.—Hysteria: blepharospasm. Contrast these two pictures with the picture of ptosis (Fig. 405) (Neurologic Department, Massachusetts General Hospital).

observed in health and in choleraic conditions, but whose genesis is still obscure, belongs to this group.

(c) Contractures

When a joint becomes more or less permanently fixed from contraction of the muscles around it, so that active or passive movements are difficult or impossible, the condition is called *contracture*. The increased tension of the muscle may depend upon increased tonus, *i. e.*, an active (although reflex) contraction, so-called *active* or *irritative contracture;* or it may depend merely upon a nutritive shortening of the muscle, *passive contracture.*

Active contractures are very closely related in their origin to tonic convulsions, and are to be distinguished from the latter only by their relative permanence. In contrast to *passive contracture, active contracture* disappears under ether or chloroform; it ordinarily diminishes during a warm bath. Even without narcosis *active contracture* may be sometimes, though not always, overcome by gentle manipulation. Such contractures offer a somewhat elastic resistance to passive movements; they are practically always associated with increase in the corresponding tendon-reflexes; every brusque attempt to overcome the contracture reflexly increases the tension; the muscles exhibit no signs of atrophy; and the contractures exhibit spontaneously a certain slow change or even a gradual transition to tonic convulsions.

Passive contractures, on the contrary, are decidedly resistant to passive movements. They are not especially influenced by chloroform nor

Fig. 374.—Same patient, showing an attempt to open left eye. Note the associated movements of the muscles supplied by other branches of the facial nerve. (See pp. 960 and 1075.)

by warm baths, and they are ordinarily associated with diminution of the tendon reflexes. If overcome by force, which is possible only by a tearing of tissue, they may disappear for a long time. This is a very rare occurrence with active contractures, except the hysteric. For the differentiation of active and passive contractures, Crocq recommends the application of the Esmarch bandage, which, like anesthesia, has no effect upon passive contractures, but causes the active ones to disappear.

Fig. 375.—Tetany in an infant eleven months of age (Dr. Gannett, Massachusetts General Hospital).

Active contractures may occur whenever the muscle tone is increased. Since the muscle tone is of reflex origin, this comes, on the one hand, from involvement of the reflex inhibitory fibers, situated probably in the pyramidal tracts, and, on the other hand, from increased irritability of the reflex centers; therefore, we generally find active contractures associated with lesions of the pyramidal tracts. They cause the characteristic appearance of spastic paralysis. Active contractures usually fix the upper extremities in a position of flexion and the lower extremities in extension, at least in ambulatory cases.

This is probably referable to the physiologic ascendency of the affected muscles over their antagonists, and to the predominance of flexor paralysis in the lower and extensor paralysis in the upper extremities. To explain the varying relations of the flexor to the extensor muscles in active contractures, Mann[1] assumes that the reflex inhibitory fibers for the flexors run with the psychomotor fibers of the extensors, and the inhibitory fibers for the extensors with the motor fibers for the flexors, or, which the author thinks more probable, are identical with them. This supposition coincides very well with the facts demonstrated by Sherrington and Herring (Physiologic Congress in Cambridge, 1898), by means of a very striking experiment on the ocular muscles, that cortical stimulation of a muscle exerts an inhibitory influence upon its antagonists. Consequently a lesion of the pyramidal tract, causing a preponderance of the paralysis in one muscle group, leads to the preponderance of the contracture in its antagonist. Attention must be called to the fact that the typical graded differences between flexor and extensor contractures may be found even in complete

Fig. 376.—Tetany in an infant eleven months of age (Dr. Gannett, Massachusetts General Hospital).

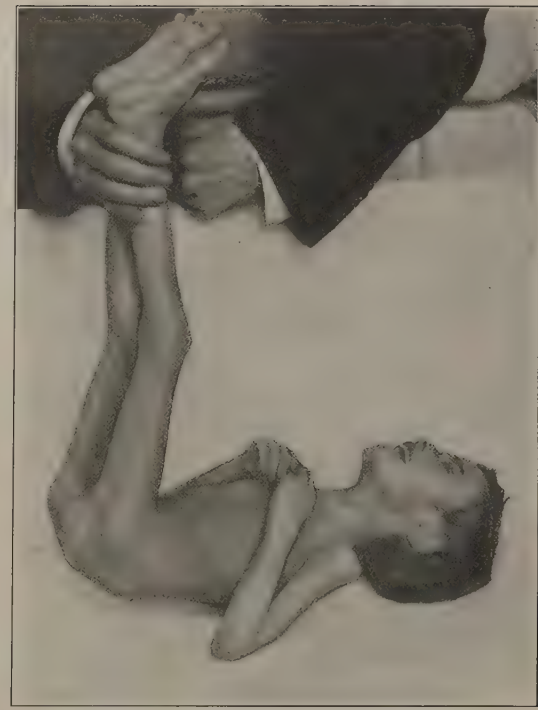
paralyses of an extremity in which there can be no question of a variable degree of involvement of the pyramids for the agonists and antagonists. As Lazarus very properly emphasizes, the physiologic preponderance of power in any one muscle group is sufficient to explain the increased contracture in that group; the more powerful the development of a muscle group, the greater the effect of the reflex increase of tonus.

The contractures in the lower extremities of bed-ridden patients, so frequently seen in transverse lesions of the cord (multiple sclerosis or lateral sclerosis), differ strikingly from those of ambulatory patients. In the former we find extensor contractures in the peroneal group (talipes equinus) only, whereas the knee- and hip-joints are flexed. Although a satisfactory explanation for this has not been given, the author conjectures that the phenomenon is due to the fact that these patients hardly ever exhibit merely contractures, but that they also evidence tonic convulsions of reflex origin which produce flexion of the legs from time to time. They remain in this state for a long time, because of the existing paralysis. In other words, the active contracture is combined with a passive contracture due to a shortening of the muscles. Passive contractures probably assist in the production of equinovarus by downward pressure of the bed-clothes upon the tip of the foot.

[1] Monats. f. Psychiatrie u. Neurologie, 1898, vol. iv.

PLATE II.

Kernig's sign in a case of cerebrospinal meningitis. Note the contractures of ham-string muscles, the retraction of the head, the expression of suffering produced by the examiner's effort to extend the lower leg, and the pronounced emaciation (Harlem Hospital, Dr. R. G. Wiener).



Faulty method of determining Kernig's sign. The thighs should first be flexed upon the abdomen before the examiner attempts to extend the lower leg upon the thigh (see accompanying picture).

A simple interruption of the reflex inhibitory tracts does not seem sufficient to explain the origin of pronounced active contractures. Muscle tonus and tendon reflexes, which pass along the same reflex paths, are generally increased in mere interference of spinal-cord conduction with a lesion of the reflex inhibitory tracts, especially in moderately paralyzed muscles (see p. 992); but a pronounced contracture appears only when a descending degeneration of the pyramidal tracts is superadded. For some unknown reason only descending degeneration seems able to cause active contractures. Perhaps it may be explained by assuming that the lower end of the inhibitory paths, *i. e.*, the pyramidal tracts, even when separated from the source of the inhibition (the central apparatus), still exerts a certain inhibitory influence upon the muscle tone, an influence which does not entirely disappear until after the tract is degenerated down to its lowest termination in the motor ganglion-cells of the anterior horns. Still another factor must be considered to be responsible for the gradual increase of the contracture after the interruption of the pyramidal tract, although such increase runs a parallel and synchronous course with the progressive degeneration of the tract. This factor is the nutritive shortening of the muscles resulting from the prolonged increase of the muscle tonus. Hence, a passive contracture is added to and intensifies at its very onset the active contracture due to the increased muscle tonus. When active contractures depend upon an anatomic lesion and are not purely functional, as in hysteria, they furnish an important sign for the diagnosis of *descending secondary degeneration of the pyramidal tracts, both in the brain and in the spinal cord* (*cerebral hemorrhage, softening, tumors, transverse myelitis, cervical hypertrophic pachymeningitis,*[1] *syringomyelia, compression of the spinal cord*, etc.). The contractures may arise in a similar way from primary systemic degeneration of the pyramidal tracts (*spastic paraplegia, amyotrophic lateral sclerosis*, etc.). The mechanism of hysteric contractures is not yet fully understood, nor is the early (at times almost instantaneous) occurrence of contractures of the paralyzed extremities (contractura præcox).

Kernig's sign, an important sign in meningitis, belongs to the class of active contractures. When the patient lies flat in bed, there is no contracture; in the sitting posture the legs can no longer be extended at the knee. In other words, the aforesaid contracture appears during meningitis, when the thigh is moderately flexed (no more than at right angles[2]) upon the trunk. It can be demonstrated either by the flexion of the knees, which appears when the patient sits upright, or by the resistance to extension at the knee-joint when the patient is seated on the edge of the bed, with the thighs at right angles to the trunk. There is a difference of opinion concerning the diagnostic value of this sign in meningitis; although Kernig has expressed himself strongly in its favor in a recent publication.[3] Kernig's sign and opisthotonos in meningitis are really due to increased muscle tonus, although the two phenomena do not run a parallel course. A further explanation is that, in healthy individuals, there is a tendency, during flexion of the thigh,

[1] Contractures in cervical hypertrophic pachymeningitis are usually the result of pressure upon the anterior and posterior roots, and hence they belong rather to the type observed during peripheral neuritis.

[2] Since with pronounced flexion the phenomenon also appears in health.

[3] Zeit. f. klin. Med., 1907, vol. xx, pp. 1, 2.

to flex the leg by means of purposeful associated movements (especially on sitting in bed), on account of the biarticular flexors of the leg, which are stretched when the thigh is flexed (hamstring muscles). Whenever the tonus is increased, an increase of this associated innervation must come into play.

According to Rostowzew, Kernig's sign can be the first sign of a beginning tetanus.

Passive contractures may occur wherever the insertions of a muscle are permanently approximated, so that the muscle is gradually shortened in a nutritive sense. This occurs *in mechanical fixation of joints* by bandages which have been applied for a long time or in surgical affections, and *localized atrophic paralyses, e. g., infantile paralyses.* In the latter, non-paralyzed antagonists acquire preponderance because of their tonus, dislocate the affected limb permanently in their own direction, and thereby shorten themselves, in the nutritive sense. There is still another type of passive contracture, which arises from contracting connective tissue, which gradually takes the place of a paralyzed and degenerating muscle, and which overcomes the tonus of the weaker antagonists. Here, of course, the contracture is not in the direction of the preserved, but in that of the affected, muscles.

A result of contractures is the fixation of parts which we see so frequently in certain paralyses. These deformities have been variously named according to

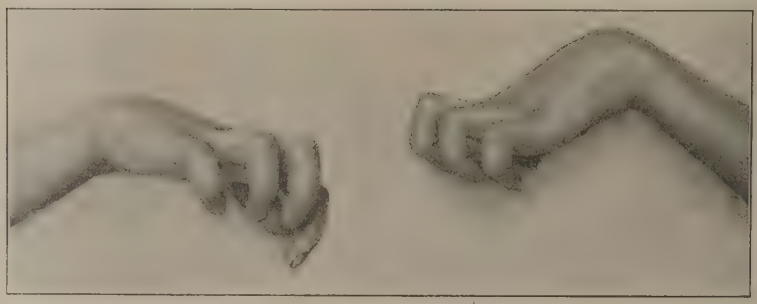


Fig. 377.—Claw-hand of ulnar paralysis.

the anomalous position of the limbs. For example, *equinovarus*, in peroneal paralyses, *claw-hand* in ulnar paralysis (Fig. 377), the *ape hand* in median paralysis, the *preacher's hand* in pachymeningitis cervicalis hypertrophica. Special pathology should be consulted for further details.

(*d*) Fibrillary Twitching (Better Characterized as "Fascicular")

These are brief clonic contractions, not of an entire muscle belly, but of mere individual groups of muscle-fibers. Outside of the small muscles of the hand and face, these contractions do not produce an actual locomotion of the insertion of the muscle, but merely a peculiar trembling or wave-like rhythmic vibration of the muscular mass. The cause of fibrillary twitching is not yet explained. It appears in paretic and atrophied muscles, particularly when of nuclear or subnuclear origin (*in spinal and neuritic muscular atrophy and bulbar paralysis*). It may also occur even without paresis or atrophy, *e. g.*, in

the *traumatic neuroses*. A certain diagnostic significance is often attributed to this phenomenon, because it is an impossible symptom to simulate; but we must be very guarded in drawing conclusions, because the action of cold upon the naked body of some healthy individuals may cause fascicular contractions.

(*e*) Tremor (Trembling)

By tremor we mean rapid and rhythmic muscular contractions which are relatively but slightly pronounced. They produce movement of the insertions of the affected muscle or the skeletal parts, thus differing from fascicular contractions. In addition to these pathologic forms of tremor, it must be remembered that, under appropriate conditions, *e. g.*, after severe physical exercise, mental agitation, intense cold, etc., tremor also appears in healthy individuals. Diagnostic importance can be attributed to tremors only after these physiologic conditions have been excluded. There are transition forms between *clonic spasms* and *tremor*, as well as between *fibrillary twitchings* and *tremor*. We distinguish between *intention tremor*, which appears only with purposeful movement, and *tremor* which persists during rest. The intention tremor is typically observed in multiple sclerosis. It was formerly regarded as a paralytic tremor, since it was assumed that the disturbed conduction transformed the voluntary impulse into a succession of rhythmic impulses (from which, as physiology teaches, the voluntary tetanic contraction is constructed), and that the muscle lost the greater portion of the separate stimuli. From his recent experience it would seem to the author that this view can no longer be maintained. He has observed that in cases of multiple sclerosis, where the increased tendon reflexes lead to clonic tendon reflexes (ankle clonus, knee clonus, wrist clonus, etc.), the intention tremor in its rhythm often closely simulates the latter. This would certainly indicate that the tremor of multiple sclerosis is nothing else than a clonic tendon or muscle reflex which is excited and maintained by the tension which the muscle experiences during the intended movement. The tremor of multiple sclerosis is consequently a spastic phenomenon, as is probably true of the majority of tremors. This conception of the intention tremor of multiple sclerosis explains why it may gradually assume the character of those less regular arrhythmic contractions which appear during the course of voluntary movements and make them simulate ataxia. The so-called rest tremor is not dependent on voluntary movement, but occurs also during rest. In fact, it may be present only during rest, and may sometimes be voluntarily controlled. This variety of tremor is one of the characteristics of paralysis agitans. It is a spastic phenomenon, the cause of which is located above the arc of the tendon reflexes, and has nothing to do with an increase of these reflexes.

To avoid overlooking tremor of any sort, we should observe patients both at rest and during purposeful movements, as well as in positions of the body which require muscular action, *e. g.*, horizontal projection of the forearm and hands with the fingers spread apart.

The characteristics of the well-known tremors are as follows:

1. The peculiarity of *intention tremor* in multiple sclerosis is that it usually ceases during repose and that it is very slight at the beginning of the movement, then gradually becomes more extensive and rapid, until it

seriously interferes with or prevents the accomplishment of the attempted movement. The excursions are frequently so large and the rhythm of the oscillations so irregular that the tremor resembles ataxia; but the attempted movement always keeps at least to its general direction. The tremor of multiple sclerosis is usually more pronounced in the upper extremities.

2. The tremor in *paralysis agitans* is relatively slow, persists during repose, is usually somewhat lessened by purposeful movements, and is inhibited, often for a considerable time, by a very strong voluntary impulse. The rate of the oscillations is usually 5 or 6 in the second. The tremor is generally noticed first in the hands, in which it is especially distinctive. It often resembles certain fine intention movements, like the rolling of an object between the thumb and forefinger. This fact would seem to indicate that the spasm underlying the tremor arises from a cerebral center in which the impulses have a partly coördinated character. The commonly observed hemilateral type of the tremor in paralysis agitans, as well as the frequent hemiplegic manifestations, favor its cerebral origin. There is rarely any tremor of the head in paralysis agitans, but to this rule there are exceptions.

3. In *senile tremor* there are 4 to 6 oscillations in the second. In less marked cases it is an intention tremor; in more marked cases it also continues during rest. The head and frequently the lower jaw, as well as the upper extremities, are the seats of this variety of tremor.

4. The tremor of exophthalmic goiter and of other *neuroses* (hysteria) is usually fine and rapid (8 or 9 oscillations to the second). It can generally be recognized most easily in the hands when they are extended horizontally with the fingers apart. Purposeful movements of the hands sometimes increase it.

5. *Toxic tremor* may assume varied forms in alcoholics, morphin habitués, in those poisoned by *mercury* and *lead*, as well as in acute and chronic nicotin-poisoning. Alcoholic tremor is characterized by early involvement of the lips, as well as of the hands. It is most pronounced during purposeful movements, and ordinarily disappears after taking a large quantity of alcohol. The toxic tremors are, as a rule, rapid.

From what has been said, there can be no doubt that tremors are essentially manifestations of spasm, even in the cases often spoken of as paralytic tremors, whenever they are associated with paralytic phenomena of the muscles. No matter how we explain tremor, it must be remembered that it also appears as a physiologic manifestation; *e. g.*, in conditions of intense excitement or fatigue. Its mechanism is physiologically performed, as it were. The author believes that tremor, just as every spasm, is to be explained by a damming up of stimuli which causes an explosive, instead of a constant, discharge of stimuli from the ganglion-cells. This is analogous to the spark discharge of an induction apparatus, in contrast to the spray-like brush discharge following low resistance. To continue the analogy to explosive discharges further, we see that the succession of impulses underlying tremors may be based on the stronger stimulation of the motor ganglion-cells; on the one hand, through the central neuron (paralysis agitans and nervous excitability) or through the reflex pathways (multiple sclerosis); on the other, because of the interruption of the current of motor impulses (peripheral palsies, fatigue, etc.). It is the same in all these cases: a disparity between the afferent and efferent nerve stimuli. This exposition is no mere hypothesis. It rests upon the well-known and generally recognized property of ganglion-cells to accumulate impulses and discharge them explosively. This peculiarity, a direct result of physiologic observation, suggests a fundamental characteristic of nerve power, for which we have as yet no further explanation. This brings us closer to an understanding of the different types of physiologic tremor.

(*f*) Choreic and Athetoid Movements

Choreic movements, or *chorea*, are involuntary, and often very extensive and excessive, muscular contractions, but, unlike clonic convulsions, they are not absolutely without coördination. They can be differentiated from voluntary movements by their bizarre character and their aimlessness. In pronounced chorea the entire body is thrown into constant motion, so that any attempt at purposeful movements is often entirely fruitless. Chorea of the facial muscles is exhibited by grimaces; chorea of the breathing, voice, and speech muscles by the choreic articulation, which may render speech quite incomprehensible. Choreic movements are most pronounced in the *neurosis chorea*, in which they constitute the principal symptom. Symptomatically, choreic movements occur in the form of hemichorea in some cases of hemiplegia, especially with lesions of the posterior part of the internal capsule and the optic thalamus (chorea post- or pre-hemiplegic).

Athetosis may be regarded as a variety of chorea. When the involuntary movements occur slowly and very regularly, the condition is called athetosis. Its significance is not essentially distinct from that of ordinary symptomatic chorea. Posthemiplegic athetosis, involving the muscles of the hand and fingers, is the most frequent form.

The muscle unrest observed in *Friedreich's* or *hereditary ataxia* is diagnostically an important symptom. French authors speak of it not unfittingly as "instabilité choréiforme." It also belongs to the symptomatic conception of chorea.

Just as in tremor, the mechanism of pathologic choreic movements is physiologically performed, and has a similar physiologic analogy. It is a well-known fact, which we can readily demonstrate on ourselves, that the organism reacts by involuntary, apparently purposeless, movements possessing absolutely the character of choreic movements, whenever it becomes necessary to maintain bodily relaxation for a long period of time. They are evidently intended (in a teleologic sense) to protect the muscles from any harm that might come through the prolonged complete relaxation. They have a voluntary component (as one may readily see) in the feeling that the movement removes unpleasant sensations in the muscles. This sensation and the resulting impulsive movement have been called *anxietas tibiarum* when they appear in the lower extremities. These physiologic choreic movements are most pronounced among the so-called nervous, highly excitable persons, and, although the voluntary component in them is recognized, they appear to be completely independent of conscious sensations and voluntary innervation. They are especially prominent when the compulsory muscle relaxation and also the surroundings at fault produce a feeling of distaste. Probably every one has experienced this who has been obliged to sit for a long time among unsympathetic, tiresome companions, or who has been compelled to attend a long, uninteresting, fatiguing lecture. We might cite, as a further example, the appearance of these movements during embarrassment or other psychic excitement. Adults gradually learn to repress these motor reactions, but their actual existence under the above-mentioned conditions can be easily demonstrated by the way an unspoiled child twists and wriggles when joked with by a stranger or when caught in a lie. The author would like to add, as a further example of physiologic chorea, the movements of the infant before it can exercise voluntary control. Later on, involuntary and purposeless coordinated movements are replaced by voluntary action, which is ataxic at first. Finally, well coördinated voluntary action takes the place of the latter. The choreic apparatus (if the expression may be permitted) persists despite this, and reappears under the physiologic conditions already mentioned, or under certain pathologic conditions. In view of the repeated localization of the lesion of posthemiplegic chorea in the thalamus, in view also of the existence of the thalamo-rubro-spinal tract (von Monakow), and the so-called quadrigeminate, anterolateral tract, which, together with the pyramids, conduct voluntary motor impulses from brain to cord, it is not improbable that the play of physiologic and pathologic choreic

movements takes place in these secondary motor pathways, and exercises, in a sense, a protective power over the muscular system. Pathologic chorea is evidently founded on an abnormal release of impulses which are in reality physiologic. Contrary to the present trend of investigation, the author believes that the most essential element for the foundation of the pathogenesis of chorea is to give the nature and point of attack of the pathologic irritation. Since we are not able to give a better explanation of the mechanism of chorea, we must consider it a preformed physiologic one. This conception of chorea, for many years adopted in the Bern clinic, renders improbable the oft-claimed, but never-proved anatomic nature of pathologic chorea, especially the post-rheumatic variety, and does not encourage the search for causal anatomic changes. Even if the determinate relation of the *occasional* embolic foci, said to have been found in the brain after post-rheumatic chorea, were established, it would not increase our knowledge of the pathogenesis of chorea. On the other hand, the assumption of an abnormal excitability for the one class of cases, and for the other, an abnormal excitation in the pathways already referred to, would explain its pathogenesis in a satisfactory manner. Might not the remaining peripheral sensory stimuli, no longer painful, but yet uncomfortable, in polyarthritic chorea be the cause of the choreic restlessness?

(*g*) Associated Movements

These are, to a certain extent, physiologic. They depend upon the fact that intense motor impulses which escape inhibition are switched off to neighboring or more distant muscle territories. Pathologic associated movements are noticed especially when, through some interruption of conduction, the impulse of the will cannot be transmitted in a physiologic direction. A weakening of the physiologic associated movements in the territory supplied by the facial nerve is sometimes of service in suggesting the existence of a paresis of this nerve quite early in its involvement.

Strümpell has described a special form of associated movement as "tibial phenomenon"; it consists of a contraction of the tibialis anticus during adduction of

Fig. 378.—Left hemiplegia, organic (combined flexion of the left thigh and trunk); inability of the left leg to remain in contact with the floor while the patient attempts to sit up or lie down with folded arms. The legs should be slightly separated.

the leg. This phenomenon is observed in spastic paralysis, and is regarded by Strümpell as indicative of an anatomic lesion in the pyramidal tract, although healthy persons may, at times, exhibit this phenomenon. It is to be regarded as having diagnostic value only when it cannot be voluntarily suppressed. According to Mann, this phenomenon may also be reversed, the leg being adducted when the tibialis anticus contracts. Other associated movements occurring with lesions in the pyramidal tract are, according to Strümpell, dorsal flexion of the great toe

during extension of the leg; the so-called radial phenomenon, which consists of extension at the wrist during flexion of the fingers; and a pronation of the hand which follows the elevation of the forearm from a dependent position, the palm having been directed anteriorly. As a symptom of a lesion in the pyramidal tract, Babinski describes an associated movement occurring particularly in hemiplegia, which consists of the elevation of the paralyzed thigh when the reclining patient sits up or simply attempts to assume a sitting posture. The latter appears to be related to Kernig's sign. (See p. 955.)

In reference to the associated movements of the eyeball in facial paralysis, which have been described as Bell's phenomenon, the reader is referred to p. 1075 et seq.

(*h*) Forced Movements

These movements, which are sufficiently characterized by their name, are highly coördinated, and so constituted that they can be simulated.

They are especially typified by most of the hysteric spasms, laughing and crying spasms, "arc de cercle," "grands mouvements," and "attitudes passionelles," as well as by many phenomena of convulsive tic. The forced movements, lateral positions, rolling and manège movements of patients with lesions of the median cerebellar peduncle belong to the same category.

A peculiar form of forced movement is the so-called forced laughing which occurs as one of the characteristic symptoms of multiple sclerosis. The laughter of these patients, whether it be spontaneous or the result of external stimuli, is spasmodic and uncontrollable; it apparently arises in the ordinary psychic way, and then, according to the statements of the patient, takes on all the characteristics of a pure somatic spasm. The fact that the forced laughing of multiple sclerosis is associated with a spasmodic condition of the musculature and increased muscle and tendon reflexes would naturally lead us to suppose that the slight motor stimulation and tension of the laughing muscles always produced by the suggestion of laughter-exciting objects or ideas, together with the increased reflex activity of the laughing muscles, is sufficient to throw the laughing mechanism into increased and continued spasmodic action.

(*i*) Catalepsy; Cataleptic Rigidity (Flexibilitas Cerea)

By catalepsy is understood a peculiar state of the motor system not yet explained, in which the limbs seem to be fixed and to present to passive motion a moderate, wax-like resistance, retaining for a longer or shorter period the position given them. Catalepsy can be differentiated from active contractures by the fact that the parts do not resume their former position after they have been forcibly changed. This cataleptic condition of the muscles occurs in the hysteric, in hypnosis (see p. 947), in the psychosis designated *katatonia*, and sometimes in brain tumors leading to stupor [especially those implicating the corpus callosum.—Ed.]. The author has repeatedly observed this phenomenon in epidemic meningitis during the period of regression.

(*k*) Myotonia

This is a rare condition of the muscles which, as yet, has been observed only in Thomsen's disease (myotonia congenita). In this affection the muscles appear normal during repose, but when voluntary movements are attempted, assume a characteristic tension which hinders the movements. The tension then gradually diminishes, enabling the movements to proceed in an approximately normal way. (See later, Myotonic Reaction, p. 1027.)

3. ATAXIA; DISTURBANCE OF COÖRDINATION AND SO-CALLED CEREBELLAR ATAXIA

To facilitate better comprehension of this section, it is advisable to read first the section upon Examination of Complicated Sensory Functions, p. 977 et seq.

Ataxia means absence or disturbance of the coördination necessary to the accomplishment of purposeful movements. Coördination is the effectual distribution of voluntary impulses to the groups of muscles which must act harmoniously in each intended movement. Ataxic movements are incoördinated or badly coördinated movements.

Ataxia shows itself clinically by movements which are not necessarily curtailed in power, but which accomplish a result different from the one expected. Ataxic movements produce an impression of insecurity; they either overshoot the mark, or, conversely, do not reach it or reach it in a roundabout way, with loss of time. The movements of a child making his first attempt at walking present the best picture of ataxia; he is not yet "master of his muscles." Ataxia is to be demonstrated clinically by observing how a patient performs voluntary movements. If the ataxia be pronounced, it may be evident in the simplest movements, because even these require coördination of various muscle groups. If less marked, it may be noticed only in attempts at more complicated and finer movements. Ataxia of the lower extremities is usually most noticeable in the patient's gait. A pronounced ataxic gait presents a peculiar rolling, swinging, frequently stamping character. Ataxia of the upper extremities may be tested by having the patient attempt to touch an object, *e. g.*, his nose with the index-finger. If he be ataxic, he will either be unable to do so, or he will succeed only after several trials. In a similar way the lower extremities may be tested for ataxia (the so-called *knee-heel test:* an attempt to touch the knee with the heel of the other foot). Ataxia, both of the upper and lower extremities, is usually increased when the patient's eyes are closed and he is thus deprived of the aid furnished by the sense of sight in correcting his movements.

Ataxia appears typically, and by far the most frequently, in *tabes dorsalis*, in *hereditary tabes*, or so-called *Friedreich's disease*, in *lesions of the motor cortex* (cortical ataxia), in *polyneuritis*, especially in *polyneuritis alcoholica*, and also in *multiple sclerosis*.

In each case the ataxia may arise from a different cause. It seems certain that in children coördination is learned essentially by the sensory control of the movements executed. A child congenitally anesthetic and blind would never learn to perform coördinate movements. Sensory control is necessary for the acquisition of coördination, and probably likewise for its preservation, although perhaps unconsciously. We may, therefore, say that the disturbances of sensibility which occur contemporaneously with ataxia have a direct bearing upon the occurrence of the latter (ataxia of sensory origin). In tabes dorsalis, which is usually associated with sensory disturbances, the conception is again acquiring prominence that these disturbances are the essential causes of the ataxia. It is self-evident that the sensibility of the skin is of much less importance than that of the deeper parts,—the joints, muscles, and tendon-sheaths,—which aid us so efficiently in determining changes of position of the extremities. (See

Testing the Appreciation of Posture and Passive Movements, p. 978 et seq.) Therefore, it follows that ataxia need not accompany a pronounced cutaneous anesthesia, provided the perception of passive movements is not affected.

In certain examples of ataxia, however, we cannot determine any coarse disturbances of the deep sensibility of the extremities, so that we must search elsewhere for the explanation. Many authors (especially v. Leyden and Goldscheider) assume, and, as the author thinks, correctly, that the disturbances of sensibility, especially in tabes, are frequently overlooked, because sufficiently accurate methods of examination are not employed to disclose the slight degrees which are present. In fact, it is conceivable that very insignificant disturbances of sensibility of joints, tendons, and muscles are quite capable of upsetting that fine control which is regulated by unconscious centripetal impulses and which persists during movement only for an instant, and yet are so slight that they might be entirely overlooked during a rough test. It should be borne in mind that, by means of the mechanism described upon p. 978, the sensation of innervation for the perception of passive movements of the extremities may also be utilized.

Even after excluding these cases with sensory disturbances which are rather minute and difficult to demonstrate, there still remain other cases in which such an explanation does not apply, and for which, therefore, we must work out some other of the explanations which follow deductively from the theory of ataxia.

Coördination, as we have seen, is accomplished to a certain extent after the manner of a reflex, using the word reflex in its broadest sense. We must assume that peripheral stimulation incites the central organs to transmit, throughout the duration of the movement, just the appropriate amount of motor stimulation to each muscular district concerned. Obviously, such a procedure may be damaged either in the sensory limb of the reflex arc, in the psychomotor center, in its immediate neighborhood, where the centripetal stimulation is transferred to the center, or, finally, in the motor limb of the reflex arc. Injury of any one of these components will probably produce ataxia.

In the so-called *cortical* or *central ataxias*, which are observed in focal lesions of the motor convolutions unaccompanied by sensory disturbances, we must assume that the cortical centers have lost their capacity for carrying out normally coördinated representations of movements and impulses. This form of ataxia, therefore, must be referred to a disturbance of the motor impulses or the sense of innervation. (See p. 972.) We cannot, however, exclude the possibility of such ataxias arising from an imperfect transmission of the centripetal sensory impulses to the motor center, for an imperfect transmission is quite possible, even if the sensory appreciation itself seems normal. Whenever an ataxia of cortical origin is also associated with sensory disturbances for the appreciation of passive movements, the latter difficulty alone is quite sufficient to account for the ataxia, just as it is in tabes. In such cases the only distinction from tabes would be that in the cortical variety the sensory path would be affected much nearer to the motor center than to the periphery. As a rule, those cortical ataxias are not very pronounced, at least in so far as they depend upon an extensive lesion of the motor cortex, because if the cortical lesion be very large, the picture of the paralysis overshadows that of the ataxia.

(Consult p. 974 in regard to the character and recognition of the ataxia due to disturbances of the representations of movement.)

A lesion in the motor limb of the "coördination arc" may also produce *ataxia*, as is well shown by the cases of motor polyneuritis without sensory disturbances. It is clear that a coördinated impulse can accomplish its proper action only when the conduction is perfect, even down to the muscles. If certain ramifications of the motor conduction be affected by serious obstructions, the coördinated impulse is naturally curtailed and ataxia must result. Under these conditions an indication of some motor paralysis would, from the nature of things, be present, and many writers are inclined to exclude such an ataxia with paresis from the true ataxias, and to call it a *pseudo-ataxia*. The author does not consider this justifiable. The characteristics of these cases may be exactly the same as of those of other origin, and even the theoretic difference exists only in a different localization of the interruption of conduction within the aforesaid reflex arc. Moreover, we must assume an interruption of conduction also both in ataxias of sensory origin and in the cortical or central ataxias independent of sensory disturbances. Besides, in cases of polyneuritic ataxia, where the motor limb is involved, the paralysis is sometimes very much in the background or can hardly be observed at all. To be sure, such a paralysis could always be detected if we were able to test the motor power of each muscle individually; but this is not possible, because in general we can test muscles only as groups. Hence slight paresis of individual muscles may readily escape our notice, although it suffices to explain the ataxia. Ataxia may even be caused by mere diminution in the tone of certain groups of muscles, from peripheral disturbances of conduction which cause retarded action of these muscles. This clinical picture of a peripheral conduction ataxia really harmonizes completely with the conception of ataxia, and plainly does not deserve the name pseudo-ataxia.

We know that the fibers of the pyramids split up in the cord into collaterals, in a manner similar to the sensory fibers of the posterior columns, and that only these collaterals, as terminal arborizations, are in contact with the anterior horn cells. Hence it becomes possible that a partial lesion of the pyramidal tract in the region of these collaterals may cause an imperfect distribution of motor impulses and produce ataxia.

The above explanation postulates coördination as a complicated reflex which is centered in the cortex. In opposition to this conception, Cyon has attempted to localize the coördinating reflex center in the spinal cord. His hypothesis not only fails to explain cortical ataxia, but is also opposed to our idea of the simplicity and elementary nature of the spinal-cord reflexes. Yet it must be acknowledged that, inasmuch as it determines muscle tonus, the spinal cord does play some part in coördination, because a muscular action takes place promptly and securely only when the muscle at the beginning of its contraction possesses a sufficient degree of tension.

Our hypothesis, nevertheless, does not admit of a special coördinating center in the brain distinct from the motor centers of the cortex, and from this a centrifugal, coördinating tract descending through the cord. Many writers, however, have assumed this. The truth is that all our knowledge of the function of the cerebral cortex, especially our

views upon motor aphasia and the results of stimulating the motor cortex in animal experiments, shows that the cortex is the motor organ of highest development, and that it sends out impulses which have been already coördinated. If, however, as is practically certain, the psychomotor or pyramidal tract transmit coördinated impulses as a direct radiation from the cortical motor center, it is quite incomprehensible what there is for special coördinating centers and coördinating tracts to do. The theory that the degeneration of the posterior columns in tabes involves a special centrifugal coördinating tract, and so leads to ataxia, is thus disproved, even if we disregard wholly the fact (which has been proved both anatomically and experimentally) that the posterior columns are nothing but prolongations of the sensory roots. As a matter of fact, this theory, opposed to the attribution of ataxia uniformly to disturbances of sensibility, was advanced only to explain cases of tabes in which ataxia was found presumably without sensory disturbances. But even if we disregard the probability of having overlooked slight disturbances in sensibility of the deeper parts (especially emphasized by v. Leyden), these cases are easily explained by assuming that the ataxia depends either upon involvement of the representations of movement in the motor cortex or upon lesions of the peripheral motor tracts. Pathologic changes have been found both in the cortex (Jendrassik, see p. 974) and in the peripheral nerves of tabetic patients. As has been mentioned, ataxia may also depend upon a disturbance of muscle tonus. This latter, which is ordinarily very striking in tabes, can readily be explained by the lesions of the reflex collaterals and of the posterior columns, even without any sensory disturbance.

So-called "*cerebellar ataxia*" requires special mention, as symptomatically it does not agree with the picture of ataxia described above, nor can it be explained in the same way. It may be described as a characteristic reeling, both in walking and standing, which is observed especially in patients with cerebellar tumors, particularly when the vermis is involved. This staggering gait, resembling that of a drunken person, is quite different from the gait of the true tabetic. It results from the disturbance of equilibrium which occurs in cerebellar diseases, and is attributed to the relation of the cerebellum to the semicircular canals by means of the vestibular nerve, and also to certain centripetal pathways of the cord (direct cerebellar and Gowers' tracts). *Cerebellar*, as contrasted with true, ataxia is associated with vertigo, and for the most part is noticed chiefly while the patient is walking or standing; whereas, while he is lying in bed, the movements of the legs, as well as those of the arms, may appear quite normal.

There is, however, sometimes a distinct uncertainty in the movements of the arms and legs even in bed, which is suggestive of tabes dorsalis. This will be understood if we remember that no extensive movement of the extremities is possible without some more or less vigorous participation of the sense of equilibrium on the part of the cerebellum in order to correct the altered relations of gravity. The changed muscle tonus, which is almost always demonstrable in these cases, may also play a part in this true ataxia of cerebellar disease. This association of change of muscle tonus with cerebellar affections has been explained by the work of Luciani, which shows that the muscle tonus is diminished by extirpation of the cerebellum. It has previously been pointed out (see p 964) that a diminished muscle tonus may produce ataxic phenomena. We consequently see that the so-called cerebellar ataxia is made up of two components—the disturbance of equilibrium and actual ataxia. The latter, however, has its own pathogenesis, quite distinct from the usual form of ataxia.

The gait is similarly affected when those centripetal stimulations essential to its rôle as the organ of equilibrium are not transmitted normally to the cerebellum, *e. g.*, in *eye-muscle paralysis* and in *affections of the organs of hearing* which lead to vertigo, especially in *affections of the semicircular canals* (Ménière's disease). The same thing is seen in *hereditary ataxia*, in which it is probably due to the loss of the centripetal impulses conveyed to the cerebellum through the direct cerebellar tract and the tract of Gowers.[1] The posterior columns are usually degenerated in Friedreich's ataxia similarly to tabes dorsalis. We, therefore, find, in addition to the manifestation of cerebellar ataxia, certain other ataxic conditions which correspond completely to tabes dorsalis.

III. GENERAL DISCUSSION OF THE METHODS OF TESTING THE SENSIBILITY

The method of testing the higher senses will be described in the part devoted to the special examination of the cranial nerves. Here we mention merely the testing of the common sensibility, especially of the trunk and extremities.

The work of M. Burchardt, referred to upon p. 1039, should be consulted in regard to the simulation of sensory paralysis, and also p. 969, concerning the impossibility of simulating certain results obtained by testing the pressure sense with von Frey's "irritation hairs."

Remarks on the Selection of Methods for Testing Sensibility.—The author purposely refrains from describing the more delicate methods for testing sensibility, such as Weber's tactile rings, Sieveking's esthesiometer, or the especially constructed thermesthesiometers; although an especial accuracy is claimed for them. This is because he believes diagnosis must depend merely upon gross changes easily demonstrated by the simplest methods. Besides, we either lack a normal physiologic standard or it is so variable with the individual that the apparent precision resulting therefrom may of and in itself lead to erroneous diagnostic conclusions. Finally, such methods require extraordinary patience and persistent practice which cannot be obtained by the ordinary practitioners. Von Frey's method of using test hairs (see p. 968) has a far better outlook.

SENSORY PARALYSIS

Complete abolition of the sensibility of a definite part of the body is called *anesthesia;* a mere diminution of sensibility, *hypesthesia.* In all examinations for sensory defect it is important to have the patient shut his eyes, in order to exclude any visual control of the results, intentional or otherwise.

The examination is complicated, because it includes the determination of the relations of very different sensory functions.

[1] The anatomic foundation for the cerebellar manifestation in hereditary ataxia should also be sought for in pathologic changes in the vestibular nerve or its terminations in the semicircular canals. Such an examination, so far as the author knows, has not yet been made.

(*a*) Examination of Simple Sensory Functions

Method of Testing Tactile and Pressure Sensibility.—Tactile and pressure sensibilities are identical in character. Pressure sensibility is nothing more than a quantitative estimation of the sensation of touch. Conversely, the examination of tactile sensibility furnishes a merely qualitative estimation of the pressure sense. Among other things in favor of this conception is the circumstance that both senses are localized at identical points of the skin—the so-called pressure points. (See below.)

Tactile sensibility is tested by touching the patient's skin lightly with the tip of the finger, or, in finer tests, by means of a dry camel's-hair brush, and ascertaining whether he feels the touch or not; if so, what he feels and where he feels it. Anesthetic spots can then be marked upon the skin with a dermatographic pencil (p. 217), and the result afterward transferred to a diagram of the body. By means of this test we can sometimes determine *a complete loss of tactile sensibility* over a considerable area; in other cases we can gather from the patient's statements that he appreciates the touch, but less plainly than normal, showing only *a slight diminution of tactile sensibility*. The comparative examination of different symmetric parts of the body is here of the greatest importance. (In regard to the significance of so-called tactile *hyperesthesia* or, better, *hyperalgesia* to touch and of the hyperalgesic zones, compare the section Sensory Irritative Phenomena, p. 982 et seq.)

Fig. 379.—Eulenberg's baresthesiometer.

Pressure sensibility or perception, *i. e.*, the quantitative appreciation of the sense of touch, can be tested accurately only when the skin has a firm support, *e. g.*, over the tibia, ulna, and radius. The part to be examined must itself be immobilized. Otherwise, to appreciate the pressure, a patient would make use of his muscular power by balancing, *i. e.*, the innervation sense (see p. 972 et seq.), and the results would no longer be correct. Gross disturbances may be recognized accurately by simply touching the patient's skin with the finger-tip, varying the amount of pressure and having him describe what he feels. For more exact quantitative determination small objects of the same bulk, but of different weight, or, still more accurately, the *baresthesiometer* (Eulenberg's, Fig. 379) may be employed. This is a simple instrument in which a pelotte (*a*) working upon a spring is applied with varying degrees of pressure to the skin, and the grams of pressure employed can be read upon the scale. By means of this instrument we can determine, on the one hand, the minimal amount of pressure which can be appreciated as differing from a mere touch, and, on the other hand, the amount of the pressure difference that can be felt, *i. e.*, how much the indicator moves before the patient can be sure that the pressure has been increased.

Von Frey[1] has found that the value of the pressure appreciation depends essentially upon the size of the area pressed upon and upon the rapidity of the pressure. The second factor can neither be exactly estimated nor regulated by simple clinical methods, hence the results of the above method are merely approximate. In any case they are of value only if the deviations from the normal are quite striking. It is at all events desirable, in order to establish such deviations, that both the patient and a normal control individual be examined exactly in the same way, *i. e.*, with corresponding areas of skin and equal rapidity of pressure.

In regard to the differences of the value of the pressure appreciation, Weber found that, normally, differences of weight of 1 : 30 can be distinguished by the palmar surface of the third phalanx of the index-finger (excluding the balancing movement, *i. e.*, with the finger lying upon the table). This relation remains almost the same, according to Fechner's psychophysical law, if we alter the absolute size of the burden within wide limits. The rapidity of the pressure probably influences these conditions. Although neglected by Weber, it should be taken into account in making comparative tests. His estimates are based upon quick pressure. In consideration of the insufficient data upon the physiologically normal values, it is advisable for clinical purposes to make control tests upon the corresponding cutaneous areas of a healthy individual under absolutely identical conditions (the same pressure surface and, as nearly as possible, the same rapidity of touch). If the affection be unilateral, it is possible to test the pressure sense by a simple, unobjectionable method. Equal weights (of identical surface and material) are placed as slowly as possible upon symmetric parts of the skin, and the patient, with closed eyes, determines whether one of the weights seems heavier than the other. Unsymmetric cutaneous areas vary so decidedly, even physiologically, in the refinement of their pressure sense, that it is not safe to employ the above-mentioned method of comparison except with the greatest care.

So-called Pressure Points; von Frey's Irritation Hairs.—The quantitative estimate of the pressure sense has been placed upon an apparently more secure basis, since we have known (Blix, Goldscheider) that the pressure sense is not scattered diffusely in the skin, but that it depends upon localized organs. The projections of the latter upon the surface of the skin are called "pressure points," and their anatomic substratum, according to von Frey,[2] consists both of the wreath-like arrangement of nerve-fibers around the hair-follicles, and the Meissner corpuscles. The pressure points are distributed in widely differing numbers to the different parts of the skin. The enumeration of the hairs generally determines the number of pressure points, because a pressure point lies in the projection of each hair-follicle, and about 95 per cent. of the skin surface is covered with hair. As a matter of fact, there are some pressure points between the hairs and upon hairless places, *e. g.*, they are specially numerous in the palm of the hand and in the sole of the foot. (On the palm of the hand, according to von Frey, there are at least 100 pressure points to each sq. cm.) These isolated pressure points are the only receptors of tactile and pressure perceptions A slight touch or pressure carefully localized between them either cannot be appreciated at all or can be appreciated only when the skin is so deformed by the pressure that neighboring pressure points are affected. Von Frey claims that the existence of localized pressure points thus renders possible a strictly localized testing of the pressure perception, and his examination seems to furnish much more trustworthy results than surface testing. In testing pressure points, we first determine the location of the points and then estimate their ability to discriminate pressure. Von Frey's irritation hairs accomplish both purposes most efficiently. They are short spears of hair of varying stiffness, glued at right angles into the end of a wooden handle. Human hairs are employed for weak stimulation, and horses' hairs for strong stimulation. Hairs have two advantages for the mechanical irritation of the skin. In the first place, they act upon very small surfaces of the skin, *i. e.*, they are sharply localized, and, in the second place, the intensity of the irritation can be graded. To estimate the hair's irritation value, we first determine the amount of weight in one scale of a delicate chemical balance which the hair can lift by exerting pressure with its end upon the other scale. The power of the hair, a term which von Frey applies to the weight raised by the hair, is a constant factor for each irritation hair, because a pressure sufficient to balance a heavier weight would bend the hair and consequently diminish its power. By means of such irritation hairs the pressure points cannot only be mapped out, but also sharply localized and quantitatively

[1] Von Frey, Untersuchungen ueber die Sinnesfunctionen der menschlichen Haut, Abhandlungen der mathem.-physischen Classe der königl. sächs. Akademie der Wissenschaften, 1896, vol. xiii, No. 3, Leipzig. [2] Ibid.

stimulated. The irritability or pressure susceptibility of a certain pressure point is to be estimated by determining the weakest hair which can be felt at that point. With hairs of different thickness the diameter, as well as the power, influences the variation of the irritation value, and von Frey has found that the irritation value is proportional to the product of the power and the radius. This product he calls *tension value*. It accordingly measures the pressure irritation value of the hair. Von Frey found the mean susceptibility of the pressure points he examined to equal a tension value of 1.44 gram-millimeters.

The power of any hair will also depend upon its length, since a long hair will be bent by less force than a short one, and it is upon this principle that von Frey's esthesiometer has been constructed. The instrument consists essentially of a strong irritation hair (horsehair), which can be pushed out of a sheath to a greater or less distance, and whose length can be read in millimeters from a scale on the sheath. The millimeter scale is gaged empirically by estimating the power of the projecting portion (by means of a delicate chemical balance) for every fifth or tenth division of the scale. The instrument is manufactured by Zimmerman, of Leipzig. The thickness of the hair must also be measured in order to determine accurately the pressure value of the instrument for a definite length of hair. The radius, multiplied by the power, gives the *tension value* of the hair, which, as mentioned above, is identical here with the irritation value. The examination of the pressure sense should be conducted as follows: The positions of the pressure points are first localized with stronger irritation, and then their susceptibility to pressure estimated with weaker irritations. As yet no clinical experience has been tabulated with this method, but it would seem to the author to possess considerable utility, although less for examining anatomic lesions of the nervous system, wherein only the grosser disturbances are of diagnostic value, than for the examination of *neurasthenic* and *hysteric symptoms*, for the investigation of the action of drugs upon the sensory nervous system, and the like.

Von Frey believes that by means of this method we can demonstrate the oscillating character of the pressure sense, *i. e.*, the periodic increase and decrease of the perception, and even its fatigue. The method may, therefore, perhaps obtain a similar significance as to the demonstration of the fatigue of the visual field in neurasthenia and hysteria. As contrasted with the latter test (visual field), the results obtained by means of the irritation hairs can in no way be simulated, because the patient is unable to orient himself concerning the pressure points that are being stimulated. Von Frey states that the mean irritability of the pressure points over the entire body is about equal. This is interesting and important for the clinical utility of the method. The local variability of the acuteness of the pressure sense seems to depend more upon the number of pressure points. The rapidity of applying the irritation hairs has but little influence, yet it is better to do it as slowly as possible.

Method of Testing the Cutaneous Sensibility to Pain.—By pricking a patient with a pin, we determine whether the prick as well as the touch is felt and properly localized. It is best to mark the anesthetic and hyperanesthetic spots upon the body and transfer them later to a diagram. In this test special attention should be paid to any delay in transmission of the impression, such as is so common in tabes dorsalis and peripheral neuritis. A good plan is to have the patient call out the word "now" the instant he appreciates the touch, and the word "prick" the instant he appreciates the prick. A distinct interval often elapses between the two. Von Frey's[1] researches attribute this difference to the increase of a physiologic peculiarity of pain perception, which, in so far as it is mechanically discharged, always possesses a distinct latent stage, which does not exist in tactile perception. It is a well-known fact that the pain caused by stubbing the naked toe becomes more severe after the lapse of an instant. The accentuation of the pain sense, the painful after-sensation, and the repetition of a painful impression (successive polyesthesia) dependent upon a slight prick are all related to this delay and occur under similar conditions.

[1] Loc. cit., p. 242.

Simultaneous polyesthesia is a different phenomenon, and probably depends upon an irradiation or a reflex perception. (See p. 983 et seq.) In this variety several pin-pricks are simultaneously perceived at neighboring spots instead of one single pin-prick. The examination with the pin-prick can be made easier by comparing different parts of the body.

Testing the Sense of Pain by Means of Irritation Hairs; Pain Points.—Von Frey[1] has demonstrated that the appreciation of pain, like that of touch, is not diffused over the skin, but is localized at circumscribed points -the so-called *pain points*.[2] The territory between these points is insensitive to pain. Ordinary experience with pin-prick at first makes this seem paradoxical until we recall that any sharp mechanical irritation of the skin sufficient to excite pain causes a deformity upon every side. To demonstrate the pain points von Frey has employed the irritation hairs described upon p. 968. The pain points are situated very close together, so that very fine hairs are selected, in order to avoid the skin deformity which would otherwise prevent an isolated irritation; they must, however, possess relatively considerable strength (see p. 968), so von Frey sharpened horsehairs by mean of a scalpel under a lens. Experience shows that for demonstrating pain points they are superior to needles, because they do not injure the skin. Such pointed irritation hairs, if possessed of sufficient "power," cause pain, which proves that the painful irritation of the skin from needle-pricks does not depend upon the injury as such. If we sharpen the hair, we can employ the esthesiometer (described on p. 967) to test the pain points. Only by employing these irritation hairs can we be positive that a painful impression is produced immediately at a definite spot, without any trace of a preceding sensation of pressure. Von Frey has further found that the *irritation value* of a hair for testing the sense of pain is equal to the product of its power (see p. 967) and the square of its surface of contact, *i. e.*, its point. He calls this varying power of irritation which decides the degree of pain the *pressure value* of the irritation hair, in contrast with the *tension value*, which, according to p. 968, measures the sense of pressure. He has not yet estimated the mean pressure value of the pain points, but it varies between 20 and 150 quadrimillimeter grams. The number of the pain points varies in different parts of the body between 100 and 200 to each square centimeter. With this great profusion of pain points it is easy to understand why we have only recently learned that pain perception is localized in points. The intra-epithelial free nerve terminations of the skin are thought to be the anatomic substrata of the pain points; they are, therefore, located more superficially than the end-organs of the pressure sense.

Von Frey's researches, as we have seen, prove that actual pain-percipient organs exist in the skin. They are interesting theoretically because they show that pain, a phenomenon which otherwise we should have considered purely pathologic, has been to a certain extent anticipated by nature and has been endowed with physiologic organs. Its importance can be easily understood because the perception of pain in the skin protects the organism from impending dangers (transmitted pressure or actual injury), just as does the pressure sense. Whether the deeper organs also possess special pain nerves is not yet known. At all events, according to the statements made above, the very remarkable richness of the cutaneous pain nerves and the great distress that follows cutaneous injuries seem quite natural from a teleologic point of view.

The investigation of Lennander and earlier surgical experience have demonstrated that most of the viscera (intestine, visceral peritoneum, gall-bladder, kidneys, heart, etc.) do not react to pain after injury. It is probable, therefore, that they possess no special nerves for pain. Furthermore, it is clear that the existence of specific pain nerves would not have the same physiologic prophylactic significance it has for the skin. Whenever an internal organ is exposed to an external stimulus, the injury is done and prophylaxis would be too late; whereas the delicate perception of pain possessed by the skin protects from injury. The sharp pain which so often appears in internal organs physiologically non-sensitive (angina pectoris, migraine, gall-stones) is, therefore, most probably pathologic. It is not caused by specific nerves for pain, but rather by means of a special stimulation of sensory nerves, which in these instances reaches consciousness in the form of pain, although it is normally subconscious.

[1] Loc. cit.

[2] These pain points must correspond to special end-organs for cutaneous pain, and have their counterpart in special pain nerves, as is proved by the dissociated sensory paralysis in tabes, syringomyelia, etc.

Method of Testing the Cutaneous Thermal Sensibility.—A sufficiently accurate and very convenient method of testing the sense of heat and cold consists in breathing upon the patient's skin with the mouth wide open and again with it nearly closed. In the former case a sense of warmth, in the latter, of cold, will be appreciated, distinctly, and so characterized by healthy individuals. If any abnormality exist, its location can be represented upon a chart of the body. We can estimate the degree of disturbance more accurately by touching the skin alternately with test-tubes filled with cold and warm water, and determining at what temperatures the water can still be discriminated as cold and warm. By this method we can estimate at the same time the so-called indifferent zone of the temperature sense, *i. e.*, the temperature limits within which the tubes produce an impression neither of warmth nor of cold. These results are valuable only when symmetric parts of the body are compared, or when the results are compared with those from a healthy individual over corresponding cutaneous areas. This method is preferable to that of estimating the minimum appreciable difference of temperature, because it furnishes separate conclusions about the behavior of the nerves for warmth and those for cold. Such a discrimination is necessary, because we know that the organs of warmth and cold sensation are anatomically distinct (warmth and cold points), and that warmth and cold perception may be affected independently of each other. Statements about the minimum temperature difference are of little value, because this difference may vary considerably according to the degree of the temperature used. Fechner's psychophysical law (see p. 968) is of no use, because the ordinary thermometer scales are divided only arbitrarily, and not according to the absolute temperatures. Especial instruments for testing the temperature sense may be desirable for physiologic purposes, but they are superfluous for clinical needs, especially if the principles of examination described here be followed.

An examination of the temperature sense is much simplified and entirely accurate if the disturbances be unilateral. Objects identical in size, shape, and substance, and of the same temperature are gently and slowly placed upon symmetric areas of the skin, and the patient, with eyes closed, tells the examiner upon which side the object feels warmer or colder. This method is of less value for differentiating disturbances which are not unilateral, because non-symmetric areas generally do not have the same temperature sensibility even physiologically.

We are indebted to the studies of Blitz and Goldscheider for the demonstration that, like the pressure and pain sense, the temperature sense also depends upon the existence of localized end-organs in the skin, which are specialized for detecting heat and cold separately. The warmth and cold points coincide neither with the pressure points nor with the pain points. Their relations have thus far been of no clinical significance. Should it be necessary in any case to determine the warmth and cold points, Goldscheider's method is the simplest. It consists in touching the skin with the slightly pointed end of a metallic cylinder varyingly heated. The end-organs of the temperature sense, *i. e.*, the anatomic, substrata of the warmth and cold points, are not yet known.

The author has repeatedly observed, during the development of sensory disturbances, *e. g.*, syringomyelia, polyneuritis, interruptions of conduction in the cord, that articles which ordinarily produce a feeling of warmth in healthy individuals are pronounced cold, and, conversely, cold things are pronounced warm. In other cases warm objects are judged extremely warm, or cold extremely cold. This has

led the author to conclude that thermal sensibility operates according to the Young-Helmholtz or Hering theories of the perception and recognition of different colored lights. These two theories have overcome the great difficulty of the latter hypothesis, namely: that the retina ought to possess special end-organs for every tone or wave length, by reducing perception to merely three colors. This agrees with the practical results of the three-color process and permits us to perceive the entire spectrum. Every wave length excites in a varying degree all, or at least two, of the three sets of fibers, and thus, by means of this variability, every wave length or color is given its proper and characteristic value. Likewise we must assume that the nerves for warmth and cold are stimulated together, during perception of temperature; the former obviously more stimulated by high, the latter by low, temperatures. According to the variable quantitative mixture of stimuli to the nerves for warmth and cold, the sensation, by means of a psychologic process, becomes a thermal perception. This hypothesis explains the phenomenon of intensification or reversal of the sensation for warmth and cold under certain conditions instead of a mere thermal hypoesthesia or anesthesia, when the excitability of the nerves in question is either diminished or lost, since the sensation corresponding to the better preserved thermal fibers will thus outweigh that of the paralyzed group, or, conversely, the sensation corresponding to the latter group will be reversed.

Method of Testing the Sensation of Motor Innervation, or the So-called Sense of Strength; Judgment of the Coördination of Volitional Impulse.—By innervation sensibility is meant the ability to estimate the measure of voluntary movement impulses during the movement itself. The coördination of volitional impulses is, to be sure, dependent upon the correct sensibility for the innervation of the individual muscles. One speaks of this capacity as the sense of strength, in so far as by means of muscular power it serves to distinguish differences in weight. The designation *power sense*, or sense of strength, is really incorrect, because neither a separate sense nor special sensory nerves preside over this function. It is much more plausible to assume that the innervation sense differs from the actual sensory function by having its origin in the motor centers and not in the periphery. Probably the conscious coördinated volitional impulse itself is identical with the innervation sense (*i. e.*, the idea of a movement in progress of becoming externalized or reaching the intensity of a volitional impulse). The expression *strength sense* or "power" sense can be justified only by its brevity and intelligibility. In reality the examination of this function might be considered quite as well under motility as under sensibility.

An entirely isolated test of the sense of strength is difficult, strictly speaking impossible, because the pressure sense simultaneously stimulated by the lifted weight is bound to influence the result. For practical purposes, the test is performed in this way: Different weights are hung in a cloth sling looped about the hand, forearm, or foot, lifted by the patient, and then discriminated. At the same time the normal relations are best preserved by practising the same experiment upon control persons with healthy nerves, *e. g.*, upon the examiner. By this method we are able to determine not only the absolute estimation of weight, but also the estimation of differences in weight which, in pathologic cases, are thought to be either too small or too large, *i. e.*, misjudged. The results are of diagnostic value only when they are very striking, because people's ability to differentiate weights by the innervation sense varies, and is to a great extent influenced by practice.

In this examination two devices may be employed to aid in excluding the pressure sense. One is to make the sling holding the weight very broad, so that it will extend over as large an area of skin as possible, and so reduce the pressure sensation below the value for which Fechner's psychophysical law holds. A slight increase

then in the weight will not influence the pressure sense. The other device, supposing we wish to estimate the strength sense of the arm, is for the patient to hold the sling with the strongest possible pressure of his hand. Here, conversely, the strong hand pressure has the effect of making the sensation of pressure so strong that, according to Fechner's law, a slight addition of weight will not appreciably increase the sense of pressure, but merely that of muscular fatigue. E. H. Weber has made use of the latter device for testing the strength sense. He found that the strength sense of the arm could appreciate differences of weight of 1 : 40, whereas the pressure sense alone of the fingers appreciated differences of 1 : 30. (See p. 968.) His researches also showed that a combination of the pressure and the strength sense do not furnish much better results than the strength sense alone. The principle of test can also be applied to the lower extremities by fastening the sling which carries the weight to the leg by means of a strongly tied knot.

Besides weights, the strength sense can also be tested by means of Eulenburg's baresthesiometer (see p. 967, Fig. 379), with this difference, however, that the part to be examined, *e. g.*, the terminal phalanx of the finger or toe, must be balanced by muscular action not supported artificially. This method does not furnish us with the estimation of the sense of power exclusively, but rather the sum of the sense of power plus pressure sense.

Even excluding the influence of the pressure sense, the results of these tests do not always furnish direct conclusions upon the "innervation" or "strength sense." The discrimination of weight may be affected by disturbances of innervation sense which are localized in the psychomotor center, and by motor pareses, because in such cases an especially vigorous impulse of the will is required to lift a weight. Whether to credit a disturbance in the discrimination of weight to an actual involvement of the "innervation sense" or to an error in judgment due to motor paresis, must be determined from the results of an examination such as we have described above, and especially from the condition of the motility. Actual affections of the innervation sense must be attributed to functional or anatomic lesions in the region of the motor cortex.

The innervation sense, in so far as it is tested as a sense of strength, always refers to the entire group of muscles which together exercise the necessary coördination for lifting a weight, and any disturbance detected must affect equally the entire group of muscles in question. It is conceivable that the disproportion between the capacity of the muscles and the sense of innervation affects only individual muscles in a group. In such cases the trouble is less a disturbance of the sense of strength than one of coördination, in that one muscle receives too much innervation for the accomplishment of purposeful movement, the others too little. On reflection it will be seen that here we are in reality only considering the two cases of ataxia alluded to on p. 963 et seq., namely, cortical ataxia from disturbances of the cortical coördination impulses, and an ataxia from partial motor paralysis (so-called pseudo-ataxia). In the *cortical form* the ataxia depends upon the actual disturbance of the innervation sense; in *partial motor paralysis*, on the contrary, while the innervation sense, as such, is correct, the impulses transmitted to the muscle are quantitatively incorrect, and, therefore, the resulting ataxia simulates a falsification of the innervation sense. Before attributing the ataxia in any given case to disturbance of the innervation sense or cortical coördination, every other possible cause of ataxia must be excluded, *e. g.*, other disturbances of motility, disturbances of the sensibility of passive movements, and anomalies of the muscular tone. If the examination disclose abnormalities of the muscular sense, the diagnosis will be strengthened. Still, the presence of such anomalies

is not absolutely necessary, because the power sense of every individual muscle cannot be tested. Just this kind of cortical ataxia has sometimes been noted in focal lesions of the motor cortex. But even in tabes dorsalis, should an actual ataxia appear without any disturbance of sensibility, cortical ataxia may possibly play a part, because, according to Jendrassik's researches, this disease presents, in common with general paresis, a degeneration of the tangential fibers of the cerebral cortex.

The So-called Sense of Location, Better Described as the Ability to Localize Sensations.—There is no special sense of location, for every sensory representation has its own place, *i. e.*, it is localized or referred to a certain part of the body. Physiologic psychology claims that each sensation produces a so-called local sign in the sphere of consciousness, depending upon the fiber from which it is discharged. These local signs become indistinct if the intensity or distinctness of the impression itself be impaired. However, we scarcely notice any disturbed localization provided the impressions themselves are perfectly intact. On the other hand, indistinct impressions and inexact localizations go hand in hand. The so-called associated or reflex impressions (see p. 982), together with the indistinctness of the local signs, are much more apt to be the cause of inexact localization in diminished sensibility. Such reflex impressions arise quite readily in interruption of sensory conduction from the lateral dislocation of the impulses through the collaterals of the sensory tract.

Slight disturbances of the location of sensation are sometimes observed in parts in which the paralysis is purely motor. They are due to the absence of the daily exercise of localization and of the continued refreshing of localization by movement, and are explained by the fact that the actual conception of space and the sensation of localization are acquired ontogenetically through motility only, and consequently require motility for their intact preservation.

The power of localizing sensation is best investigated by applying the touch, pain, and temperature tests to the area to be investigated, the patient having his eyes closed, and then requiring him to open his eyes and locate with his finger the spot at which he experienced the particular sensation; or, if this be impossible on account of motor disturbances, to describe its location. The difference between the point irritated and the point indicated by the patient, expressed in centimeters, indicates the degree of the error in localization. Absolute values for the normal error in localization cannot be given, since they are subject to great individual variations and are markedly influenced by practice. It is consequently best to compare the investigated area with the opposite healthy one, or, if this be impossible, with the same region in another person of similar physical and mental characteristics. In view of the influence of practice, only marked errors in localization are of diagnostic importance.

The So-called Muscle Sense or Muscular Sensibility.—What we have described above as the innervation sense is often confused, under the common title of *muscle sense*, with the appreciation of active and passive movements, to be described later. Such a special muscle sense does not really exist, and the obscure term leading to a misconception should, therefore, once for all, be dropped.

Method of Testing Bone Sensibility; the So-called Sensation of Vibration.—M. Egger[1] was the first to demonstrate the feasibility of testing the sensibility of the bones by applying a vibrating tuning-fork to them. The examination

[1] Jour. de Physiol. et de Pathol. gén., 1899, vol. i, No. 3.

was suggested by the extreme sensitiveness of periosteal lesions. If we set a C tuning-fork of 132 vibrations or an ordinary A tuning-fork of 440 vibrations upon the surface of a bone, the person examined normally perceives a characteristic thrill or tremor. Egger believes he has demonstrated that this perception in pathologic cases is entirely independent of the absence or presence of cutaneous sensitiveness, and has proved that it is actually peculiar to the osseous system. It may be retained with a diminished cutaneous sensibility or lost when the latter is normal, despite the fact that the vibrations are naturally transmitted to a considerable distance. Egger found that this thrill was strictly localized, so that under pathologic conditions the tuning-fork was appreciated at one spot of a bone and not at a neighboring spot. He also demonstrated a hyperesthesia of the bones, for they could appreciate the vibration of a high tuning-fork (vibrating 2048 times), although this normally is not perceptible. Bone anesthesia occurs especially frequently in the ataxic stage of tabes. The occurrence of disturbances in the appreciation of passive movements is, however, independent of the bone sensibility. In many cases of tabes, and especially in the initial stage, tuning-fork vibrations produce a sensation of burning as well as a thrill (hyperalgesia of the bones). In the trophic changes of the joints and bones in tabes, the disturbances in bone sensibility are usually found in the vicinity of the affected parts. Disturbances in bone sensibility also occur in *syringomyelia*, and mostly in the diffuse areas of anesthesia so characteristic of this disease. In *Brown-Séquard's unilateral paralysis*, the osseous sensibility, like that for passive movements, and in contrast to the cutaneous sensibility, suffers upon the same side as the motor disturbance. In *cerebral hemi-anesthesia* bone anesthesia is localized upon the paralyzed side, although it is ordinarily incomplete upon the head. Bone sensibility varies in *hysteric anesthesias*. Frequently, though not constantly, the bones share in the anesthesia. In hysteric conditions the bone, as well as the cutaneous, sensibility not uncommonly suddenly reappears under the influence of the tuning-fork vibrations. Bone anesthesias sometimes of equal, sometimes of less, extent than the sensory disturbance of the skin, also are found in *transverse lesions of the spinal cord*. In the latter case the bones of the lower end of the leg are ordinarily most affected. From the pathologic findings Egger believes that the tracts for bone sensibility take an uncrossed course in the gray matter.

Egger's supposition that the vibrations of the tuning-fork are perceived only through the bones has recently been shown by Goldscheider[1] to be erroneous. The soft parts are also susceptible to these vibrations, but not to so great a degree, since they are unable to vibrate as synchronously. Goldscheider found, in contrast to Egger, that the perception of tuning-fork vibrations is partly dependent also upon the condition of cutaneous sensibility. One way in which he proved this was by anesthetizing the skin with cocain. The cutaneous sensibility and the osseous sensibility to tuning-fork vibrations may be separately tested by pressing the tuning-fork softly against the part for the former, and firmly for the latter. In the first instance the vibrations remain upon the surface, while in the second they are conducted to the deeper parts through the compressed skin. Goldscheider calls the perception of the vibrations of the tuning-fork the sensation of vibration, and regards it, not as a specific sensation, but as an expression of the sensation of rhythmic interrupted irritation of the nerves that are responsible for the sensations of contact or pressure. Rydel and Sieffer[2] call this quality of sensation "pallesthesia" (πάλλω—I shake). In spite of his objections to the conception of Egger, Goldscheider regards the test with the firmly applied tuning-fork as the best procedure for the estimation of osseous sensibility.

The author agrees with the view that the perception of tuning-fork vibrations is not a special bone sense, but rather the perception of oscillatory irritations through the nerves for touch and pressure sense in general. The specific part lies merely in the rhythmic character of the stimuli, which the bones are especially fitted to perceive in virtue of their capacity for vibrations.

We can prove that we are concerned chiefly with excitation of the nerves of touch and pressure sense, because we can demonstrate on ourselves an oscillatory quality of excitation for these nerves only. (See p. 969.)

Whether or not pain stimuli can have a similar vibratory character remains to be proved. We know, however, that certain forms of pain have the character of a vibration, *e. g.*, after contusion of the ulnar. But this is possibly due to association with the vibratory sensations of touch and pressure. Many observations have led the author to believe that the test of the sense of vibration is really an extremely

[1] Berlin. klin. Woch., 1904, No. 14.
[2] Arch. f. Psychiatrie, 1903, vol. xxxvii, p. 488.

delicate test of touch and pressure senses, which possesses clinical value by reason of this delicacy. By means of the tuning-fork, he has often demonstrated in tabes dorsalis transverse lesions of the cord and cerebral affections, sensory disturbances which would otherwise have escaped detection.

It has also proved itself of value in segmental localizations, in that, on the one hand, it alone sharply differentiated the limits of the sensory disturbance, or that, on the other hand, it overlapped the limits established by the usual test of contact sensation.

It seems that the earliest disturbance appears as an inability to perceive impulses of short duration as separate vibrations.

From this stand-point the method is to be recommended as part of the clinical armamentarium, although it cannot be denied that in some cases the ordinary test of the contact sensation betrays disturbances which the tuning-fork fails to show. These are, however, obviously exceptions. In order properly to utilize the method, tuning-forks of different vibrations must be employed, and the results of each carefully recorded. Rydel and Seiffer (loc. cit.) elaborated a quantitative method for the use of the tuning-fork. They recommended a tuning-fork provided with a Gradenigo triangular block on one arm, whose amplitude of vibration should be read at the instant the vibration ceases to be appreciated. The tuning fork most useful for this test is the C fork (128 vibrations) fitted with a Gradenigo triangle.

THE FARADIC TEST OF SENSIBILITY

Test of the Sense of Faradic Vibrations

The electric testing of sensibility has been intentionally disregarded in the former editions of this work, because the method was not sufficiently perfected, and also because we are really uncertain of what we are testing. This restriction at the present time will be applied merely to the galvanic testing of sensibility, because in this instance direct stimulation is complicated by the electrolytic or chemical stimulation of the cutaneous nerves, which is an additional factor that cannot be reckoned quantitatively. Subsequent examinations have, however, led to the conclusion that testing by means of a faradic current when the interrupter swings free has clinically the same characteristic significance as the tuning-fork vibrations, *i. e.*, it is a more delicate test of contact and pressure sensations. If the current be not strong enough to cause pain, faradic stimulation of the body surface with a freely swinging interrupter produces a sensation of vibration which cannot be differentiated quantitatively from the sensation of a vibrating tuning-fork. Since a vibratory character does not appear in qualities of sensations other than that of touch and pressure in the ordinary every-day life (see p. 975), we may well assume that the sensation of faradic vibrations, if the term may be permitted, has the same significance as that of tuning-fork vibrations, and is due to an oscillatory irritation of the nerves for touch and pressure sense. The author's investigations have taught him that the same rule holds for the faradic vibrations as for the tuning-fork; namely, that early disturbances can be detected more readily than with any other method of testing sensation. It is, however, obviously necessary that the current produce the sensation of vibration only and be weak enough to avoid every painful sensation. As soon as painful sensations appear, it can no longer be considered as an improvement of the examination, and the result will be ambiguous. For this reason we cannot use the well-known sensory electrode of Erb, which consists of a bundle of thin copper wires bound together with a non-conducting substance, the cut ends of which are placed dry on the surface of the skin. This electrode, in consequence of the condensation of current and the uncertain contact, does not readily allow us to exclude pain stimuli. The moist electrodes used ordinarily in testing motion are to be preferred. (See p. 1011.)

Many clinical observations have shown that the electric method of testing sensibility has the same value as the tuning-fork for the demonstration of differences of sensation and their boundaries in one and the same patient. It possesses certain advantages over the latter. It seems simpler from an instrumental standpoint, and one can modify conditions during the experiment by altering the strength of the current or the manner of oscillations of the interrupter, which can only be achieved with the tuning-fork by the use of a number of forks of different tones. There is this disadvantage, however, that the results of different faradic apparatus, as well as tests undertaken at different times, cannot be compared one with the other, both on account of the difference in the amount of electric energy used, and the impossibility to fix a definite standard for the number of oscillations of the ordinary inter-

rupter. Thus the results of the faradic test of the sensation of vibration are positive only in so far as they are comparative at the time they are obtained. To be sure, this degree of objectivity is sufficient to establish disturbances of sensibility and their boundaries.

The question, whether or not certain variations, founded on the difference in the quality of the stimuli, appear with the general agreement between the electric and tuning-fork tests of the sense of vibration, must be deferred until further investigations have been made.

METHOD OF TESTING THE SENSATION OF MUSCULAR CONTRACTION (Curschmann)

H. Curschmann, Jr.,[1] employs the following method for testing the sensation of the contraction of muscles (not to be confused with the sense of innervation). (See p. 972.) The extremity is placed so as to avoid, during the contraction of its muscles, any friction between the cutaneous surface and the support, thus preventing confusion with the cutaneous sensibility, and the amount of current necessary for the minimum cathode contraction of the muscle to be examined (in case of reaction of degeneration, anode contraction) is determined. The patient is told to close the eyes and see whether he can perceive a movement in the given muscle area in addition to the pricking pain of the closure of the current. If intelligent, he can distinguish between the sense of contraction of the muscle and the sense of movement of that part of the extremity. He must then indicate the appearance of the sensation of contraction during gradual increase of the current; always with the precaution that he indicate with his finger the muscle in question. H. Curschmann found that in healthy individuals the sensation of contraction has a standard value several milliampères lower than that necessary for the minimal contraction. It is never higher.

Curschmann found considerable variation from the normal in diseased conditions, *i. e.*, tabes, hemihypesthetic hemiplegia, syringomyelia. In these diseases the disturbances generally increase as we proceed from the proximal to the distal end of the extremity He considers this behavior very important in the differential diagnosis between hysteric and organic hemianesthesia. They are almost always present in the area of dissociated sensory disturbances of syringomyelia, whereas in multiple sclerosis they may be present where there is disturbance of motility or may be completely absent in spots. Where muscles show reaction of degeneration, the perception of contraction is usually much diminished or disappears.

(*b*) Examination of Complicated Sensory Functions

Method of Testing the Perception and the Judgment of Active Movements of the Extremities.—Even with closed eyes a healthy person has a very exact knowledge of every change of posture of his extremities, and graduates his motor impulses accordingly. These perceptions of movement depend primarily upon the innervation sense (see p. 972 et seq.), *i. e.*, upon the judgment of the impulses of contraction which the individual muscles receive in a certain position, and, secondarily, upon the sensibility of the deeper portions of the extremities, *i. e.*, of the muscles, joints, tendon-sheaths, and even of the skin. They are, of course, compressed and stretched differently in every change of posture. So this performance does not depend merely upon a particular sensory function, but upon the cerebral reception of several sensory impressions aided by the innervation sense, which belongs in reality to motility. Affections of the appreciation and judgment of active movements are, therefore, encountered as often in sensory disturbances from peripheral interruption of conduction as in lesions of the psychomotor centers or tracts, in consequence of an impaired harmony between the degrees of voluntary impulse and the resultant movement. Yet, when the cause of the affection lies upon the motor side, the sensibility of the deeper parts can, to a certain extent, perform vicariously

[1] H. Curschmann, Deut. med. Woch., 1905, No. 31.

the function of the impaired judgment of the condition of muscular contraction; and, conversely, when the defect lies upon the sensory side, the innervation sense can compensate a certain part of it. It appears that this vicarious performance of one function by another is possible, and varies somewhat with the individual.

To test the appreciation of active movement, we direct the patient either to describe as accurately as possible a position of his extremities, which he voluntarily assumes and alters while his eyes are closed, or to touch with an extremity an object whose position he has noted before he closed his eyes, employing the shortest and most direct movement possible. In the latter experiment any disturbance of the function in question is manifested by the ataxic character of the movement and by its lack of certainty. This test, then, is like that for ataxia. But although absence of ataxia proves that the patient judges his voluntary movements correctly, nevertheless, if ataxia be demonstrated, we require further evidence to decide that it is accompanied by a failure in the appreciation or judgment of active movements. The latter function may be absolutely preserved and the patient may be perfectly cognizant of the ataxic peculiarity of his movements with closed eyes, yet be unable to execute them coördinately if the motor elaboration of his movement impulses be defective. We need the most accurate analysis possible, and a consideration of all the conceivable causes of ataxia, in order to decide if the ataxia proves faulty judgment of the patient's own movements. Should the muscular tone (p. 964) be normal and no sign of motor weakness be present (p. 963), we must attribute the ataxia by exclusion to a disturbed central motor coördination or to imperfect impulses. Then we must decide whether such an affected judgment depends upon an actual disturbance of sensibility or of the innervation sense, *i. e.*, a faulty representation of movement (p. 963). If the former, the appreciation of passive movements will also be affected. As we have already mentioned, this is the commonest cause of ataxia. (See p. 962.) It is also worth noting that an intelligent patient, simply by his own observation, can often decide correctly whether his ataxia is due to a disturbance of sensation or to a faulty sense of motor innervation, *i. e.*, coördination impulse. Actual disturbances of sensibility are the usual causes of the ataxia in tabes dorsalis, but a disturbance in the innervation sense or in the representation of movements may cause ataxia in cortical affections, without any true disturbance of sensibility.

Method of Testing the Appreciation of the Position and of Passive Movements of the Extremities [Postural Perception.—Ed.].—In estimating a passive change in position of the limbs, the innervation sense is of no assistance. We judge of it purely in a sensory way by employing the sensibility of the deeper parts, muscles, fasciæ, joints, etc., and in part through the skin (perception of the differences in tension). Theoretically considered, the appreciation and judgment of active movements must be easier than those of passive movements, because the former utilizes more aids (*e. g.*, sense of innervation). Therefore, even where the appreciation of active movements be intact, that of passive movements must still be tested for. It is done in this way: The patient, with closed eyes, is asked either to describe passive changes of position in his extremities, or to imitate them with another extremity whose innervation has not been involved. This will not be possible if the appreciation of passive movements be affected. Yet

it is to be noted that, under some circumstances, the patient can compensate moderate disturbances by informing himself of the position of his extremities through the appreciation of muscular contractions by means of the innervation sense. (See p. 978.) In this way we may perhaps explain the frequently observed fact that the estimation of passive alterations of posture is comparatively well preserved in moderate sensory disturbances of the extremities, although this gives us no right to assume that the sensibility of the deeper parts has escaped. To obtain clear results in such cases we must demand of the patient a practically complete muscular relaxation. In most cases disturbances in the appreciation of posture show themselves without anything further by an ataxia, because of the failure of the essential sensory control of the movements. Hysteric disturbances of sensibility present an exception to this rule; in them the appreciation of posture can be completely lost without the appearance of ataxia. This can be explained by the nature of hysteria; because here the disturbance lies in the most central fields of consciousness, so that the intelligent appreciation of passive changes of position is annulled, but not the control of movements, which is supplied by the sensory impulses further down.

Disturbances in the appreciation of passive movements are observed principally in tabes dorsalis, where, as mentioned repeatedly above, they furnish a sufficient explanation of the ataxia. It is not rare to meet such disturbances in diseases of the motor area of the cortex, apparently because, for the purpose of coördination, the sensory fibers which subserve the appreciation of posture are anatomically related to the psychomotor centers. The above-mentioned disturbances in the perception of posture which occur in hysteria belong, in a broader sense of the word, as most hysteric symptoms do, to cortical manifestations.

Method of Testing the Touch Perception (the Stereognostic Sense).—Touch perception, *i. e.*, the recognition of the form of objects by their surface, is by no means, as is sometimes supposed, merely a function of the tactile and pressure sensation. Its popular title, feeling sensation or feeling sense, is, therefore, in the strict sense of the word, incorrect. In handling an object we first employ the touch and pressure sense, then the appreciation of the active movements essential to feeling the object, further the perception of the position of the fingers encircling it, and, finally, the sensation of temperature, to recognize the material of which it consists (metal, wood, etc.). Here again it is a question of very complicated perception worked out in the brain with various aids, but in no way the product of a single specific sensibility. This conception makes it clear how, even when the examination of the simple sensory functions (contact, perception, etc.) shows no disturbance at all, the stereognostic recognition of objects may be disordered in cerebral disease, *i. e.*, in lesions of the motor cortex, whose relation to the innervation sense and to the judgment of active and passive movements and of the position of the extremities has already been mentioned (see p. 972), as well as in peripheral motor paralysis, which prevents a correct appreciation of the innervation sense. Conversely, touch perception will be at least impaired where the elementary sensory functions have suffered. Still, this is not always the case because the intelligent individual possesses in a high degree the faculty to replace this defect in the perception through the imagination; in other words, to guess correctly from few guides.

To test the stereognostic sense we ask the patient to close the eyes, and name various small objects placed in his hand. This function is only slightly developed in the feet, yet a healthy individual can recognize larger objects, *e. g.*, the number of fingers with which he is touched, a glass or a bottle even, with them. Objects placed upon the trunk can be recognized only when they are very large and characteristic. This clearly demonstrates that the stereognostic sense is not essentially aided by the cutaneous sensibility, as the old name, "feeling sense," would lead us to believe. As is well known, the stereognostic sense is very acutely developed in the mouth, where it depends considerably upon the perception of the active movements and of the position of the tongue.

PHENOMENA OF SENSORY IRRITATION

Paresthesia.—By paresthesias are understood subjective sensations, *i. e.*, sensations corresponding to no correlation in the external world, which are not actually painful, but which, without any sharp boundary, often merge into pain. They are sufficiently well characterized by such names as "*furry*," "*tickling*," "*crawling of ants*," and "*falling asleep*." The interrupted character and the wide dissociation of these sensations (the latter especially characterizes the sensation of fur or crawling of ants) depend, according to the researches of von Frey, upon the oscillatory character of the nerve stimulation in pressure sensation. This can very easily be demonstrated by exciting the pressure points by irritation hairs. (See p. 968.) Subjective feelings of warmth and cold correspond to similar paresthesias in the province of the thermal nerves; those of smell, sight, hearing, and taste, in the territory of the higher senses. Paresthesias may arise from an irritation of the sensory tracts at any point of their entire course, but they are most frequently observed in lesions of the sensory roots downward, and are, therefore, localized in the peripheral nerves. The paresthesias which occur in spinal cord affections, and which are localized at the intercostal nerves or, rather, their sensory roots, are spoken of as "girdle sensation." The girdle sensation frequently becomes a "girdle pain." Paresthesias play an especially important part in the obscure clinical picture of acroparesthesia.

Spontaneous Pains.—In a general way pain may be subdivided into parenchymatous and neuralgic pains. In *parenchymatous pains* the sensory fibers are irritated at their outermost terminal ramifications; in *neuralgic pains*, at the trunks of sensory or mixed nerves, in the sensory roots, or in the sensory centers. In the *former* the terminations of the sensory fibers are irritated quite independently of their origin, and, therefore, the pains overlap the boundaries of peripheral sensory areas, apparently at will. *Neuralgic pains*, on the contrary, according to the law of eccentric projection, are localized in areas that correspond exactly to the peripheral distribution of the nerve-trunk or nerve involved. Pain may, however, be felt in neighboring nerve territories as a result of radiation. (See p. 983 et seq., Sympathetic Sensations.) A further difference between these pains is to be found in their severity. *Neuralgic pains* are generally much more severe than *parenchymatous pains*, for the reason that in the former a much larger number of fibers are painfully irritated, and ordinarily at the same moment. Probably for the same reason remissions in a severe pain are more decided in

neuralgic than in *parenchymatous pains*. Some of these remissions can readily be attributed, at least in part, to a fatigue of a central pain-percipient apparatus, a fatigue which naturally occurs sooner and more pronouncedly after intense irritation than after weaker irritation. Another distinction is that, generally, with parenchymatous pains, the entire painful area is sensitive to pressure. This is sometimes the case with neuralgic pains; but, as a rule, only that portion of the nerve-trunk is sensitive to pressure which lies superficially or upon a hard foundation (neuralgic pressure points).

The best-known example of neuralgia pains are the *true neuralgias*, which occur in some instances in otherwise healthy individuals, but which in other instances are indirectly due to disease (*articular rheumatism, syphilis, diabetes*, etc.), and the so-called *lancinating pains* in spinal cord diseases, especially in the initial stage of *tabes dorsalis*.

In regard to parenchymatous pain we should remember that internal organs which normally do not react painfully to mechanical lesions, may, under pathologic conditions, give rise to pain of the greatest severity. It would seem that, in addition to the pain depending upon irritation of special nerves for pain, which the author prefers to call physiologic pain, and which, for teleologic reasons, is limited merely to the body surface, there is a second sort of pain which depends upon the increased irritability of nerve-tracts not capable of producing pain normally. This conception involves the further assumption that certain sensory nerves not usually transmitting pain (*e. g.*, the optic and acoustic) may,,under strong stimulation, also become distinctly painful; and that this kind of severe sensory irritation is not simply a secondary effect caused by reflex muscle contraction (iris, stapedius,[1] etc.).

To the parenchymatous pains belong most of those *pains* which occur in *organic disease of various viscera;* many of the *diffuse headaches* of *meningitis* and *intracranial pressure; toxic, febrile, dyspeptic*, and *anemic headaches*, as well as *migraine* and most forms of *neurasthenic headaches*.

The author does not accept the view that internal headache must always have its origin in the dura mater In a physiologic sense the intracranial parts suffer pain merely from mechanical lesions of the dura; but the brain may behave just the same as many internal organs (gall-bladder, heart, etc.), namely, while possessing physiologically no deep pain perception, it becomes sensitive to pain under the influence of pathologic conditions. The author does not doubt that the fatigue headache of *neurasthenia*, just as well as the pain of *migraine*, is a cerebral pain, and this view is supported by the occurrence of the scintillating scotomata in migraine (see p. 1034), which are unquestionably localized in the brain cortex.

In most cases the sensation of pain, whether it be neuralgic or parenchymatous, is of peripheral origin, *i. e.*, depends upon an irritation of the peripheral sensory neurons (of the peripheral nerves or sensory roots). It still seems doubtful whether pains may be caused by involvement of the conduction tracts above the sensory roots in the spinal cord. This part of the conduction pathway has usually been considered to be purely esthesodic, *i. e.*, conductory but not irritable. On the contrary, eccentrically projected pains can doubtless be produced by lesions of the sensory tracts in the brain, especially of the most poste-

[1] [The recent studies of Ramsay Hunt (Archives of Otology,1907, vol. xxxvi, No. 4) on the cutaneous distribution of the pars intermedia of Wrisberg, the intimate connections between the acoustic and geniculate ganglia, and their relations to herpes zoster of this region, should make us cautious in accepting this view of the acoustic nerve.—Ed.]

rior part of the internal capsules,[1] as recently observed by the author in a case of hemiplegia.[2] It is also certain that pains may take their origin from the most central organs of perception. It is to this category that the *suggested* and *autosuggested pains* and certain *hysteric pains* belong. Naturally, these pains have in their distribution the character of parenchymatous not neuralgic pains, because the arrangement of the elements in the central parts does not correspond to the nerve-trunks, but to the limits of the organ. For instance, hysteric joint pains are often improperly spoken of as articular neuralgia.

A peculiar combination of symptoms, so-called *anæsthesia dolorosa*, should be mentioned here. It consists of the occurrence of spontaneous pains in a portion of the body which is anesthetic to external stimulation. Such conditions occur when a focus of disease, most often of the peripheral nerves or nerve-roots, interrupts the conductivity of peripheral stimuli and at the same time causes irritation of the sensory fibers. This symptom-complex is seen most frequently in tumors of nerves, but it also includes many of the pains of tabes dorsalis and neuritis.

Hyperalgesia (Hyperesthesia); Tenderness to Pressure.—By the term hyperesthesia or, better, hyperalgesia, we understand a condition of the sensory mechanism in which stimulation produces the sensation of pain in a certain area (especially of the skin), although normally such stimulation would not be painful. The slightest touch of the skin, moving the part, or the mildest sort of thermic influence may, under such circumstances, produce pain. We now recognize that pain perception (at least cutaneous pain perception) is a specific performance of a definite kind of nerve-fibers (see p. 970, note 2); hence, we may regard hyperalgesia merely as a supersensitiveness of the pain nerves. We have as yet no convincing demonstration that a vigorous stimulation of other sensory qualities, *e. g.*, of touch, warmth or cold, can produce pain, because we cannot exclude a coincident implication of the pain nerves in every such vigorous stimulation. Therefore, we should substitute the expression hyperalgesia for hyperesthesia. That hyperalgesia of the lower half of the body appears most readily on the same side as the lesion in spinal hemiplegia must be explained by the supposition that in pathologic conditions the pathways of other sensations, especially that of touch sense, may also give rise to painful stimuli. This occurs either by means of increased excitability of the pathways (see p. 981), or else through a narrowing of the channel for the centripetal conduction of sensory impulses, as in the author's explanation of hyperalgesia in spinal hemiplegia. (See p. 1126.) We do not yet know what sort of injury to the pain-conducting or the pain-appreciating parts of the nervous system can give rise to the usual form of hyperalgesia; but it is certain that peripheral as well as central parts may assist in this hyperalgesia, from an associated involvement of the sensory fibers or cells. Such involvement produces slight injuries, which are insufficient to induce anesthesia, but sufficient to cause irritation. The best known examples are the *hyperalgesias in the domain of neuralgic nerves during the early stages of neuritis*, the *zone-like hyperalgesias of the upper borders of sensory dis-*

[1] See the meager literature upon this point in the article of Alfred N. Reichenberg, Zeit. f. Nervenheilk., vol. xi, pts. 5 and 6, p. 349.

[2] [This is also the chief symptom in Déjérine's thalamic syndrome.—Ed.]

turbances in cross-lesions of the spinal cord, the above-mentioned unilateral hyperalgesias in spinal hemiplegias (see p. 1126), and the *general hyperalgesia of hysteric or neurasthenic patients.*

The so-called *tenderness to pressure* (better described as increased sensitiveness to pressure) is in reality nothing more than a special form of hyperalgesia. In the examination of the nervous system, the pain sensitiveness of the nerve-trunk to pressure which occurs principally in peripheral neuralgic and neuritic affections is of special interest. It is under some circumstances essential to examine into this phenomenon, even where no spontaneous pain is present.

The hyperalgesic zones of the skin in diseases of the viscera are mentioned in the following section.

Sympathetic or Reflex Sensation; Irradiation of Pain; Tickling; Hyperalgesic Zones of the Skin in Diseases of the Deeper Organs.—So-called sympathetic or reflex sensation is clearly related to hyperalgesia.

The best-known form of this is pain irradiation, in which the pain is perceived far beyond the limits of the painfully irritated peripheral part (pain in the entire trigeminal distribution, occasioned by a single carious tooth). This phenomenon can be explained only by assuming that the painful stimulation in the central organs (spinal ganglia, gray substance of the spinal cord or of the brain) overlaps or radiates to neighboring tracts by means of dendrites and Golgi's collaterals, and that, in accordance with the law of eccentric projection, confusion as to the origin of the perception results.

The pain sense is not always concerned in reflexes either of primary or of secondary nature; in fact, touch and temperature sense or the higher senses can produce them, and such sympathetic sensations are not necessarily painful.

As an example of such associate sensation *tickling* may be cited. This is an irradiating or sympathetic sensation of an oscillating character, diffused over a considerable surface of the skin, caused by a circumscribed skin stimulation.

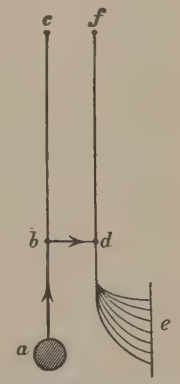


Fig. 380.—Diagram to illustrate skin hyperalgesias and the radiation of pain in disease of deeply situated organs.

Quincke[1] has made quite a complete collection of the practically important sympathetic sensations which have been thus far determined; but only a few of the most important will be mentioned: trigeminal neuralgia in affections of the frontal sinuses; parietal pain in affections of the middle ear and of the mastoid process; a tendency to cough from irritation of the posterior wall of the auditory canal (irradiation from the auricular branch of the vagus to the other vagus branches); a marked sensation of tickling and shuddering in biting upon sand; painful sensation in the back in swallowing the wrong way; laryngeal pain in percussing a pulmonary abscess (Quincke); pain in the left arm (rarely in the right) in angina pectoris; pain in the back in stomach diseases; feeling of tickling in the nose from intestinal worms; pain in the shoulder in liver affections; pain in the left shoulder in affections of the spleen; pain in the back and genitalia in renal affections; pain in the lumbar region and genitalia in bladder affections; pain in the epigastrium and the stomach region in endometritis and during menstruation; pain in the knees in coxitis; simultaneous polyesthesia (p. 969) in spinal cord affections.

[1] Zeit. f. klin. Med., 1890, vol. xvii.

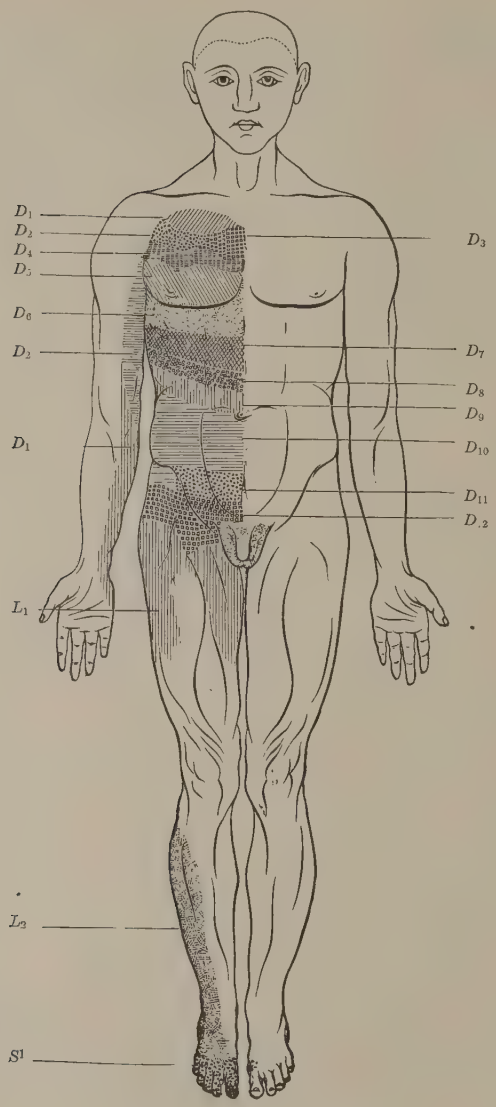


Fig. 381.—For description see Fig. 382.

A phenomenon related to and frequently associated with these sympathetic sensations—a circumscribed cutaneous hyperalgesia depending upon diseases of the deeper organs—is of more diagnostic significance. The best-known example is the sensitiveness to pressure of the skin of the precordia in heart disease. This hyperalgesia is perhaps most satisfactorily explained thus: The centripetal irritations proceeding from the diseased organs which escape direct perception, stimulate by irradiation the neighboring sensory parts of the central organ, which are inter-

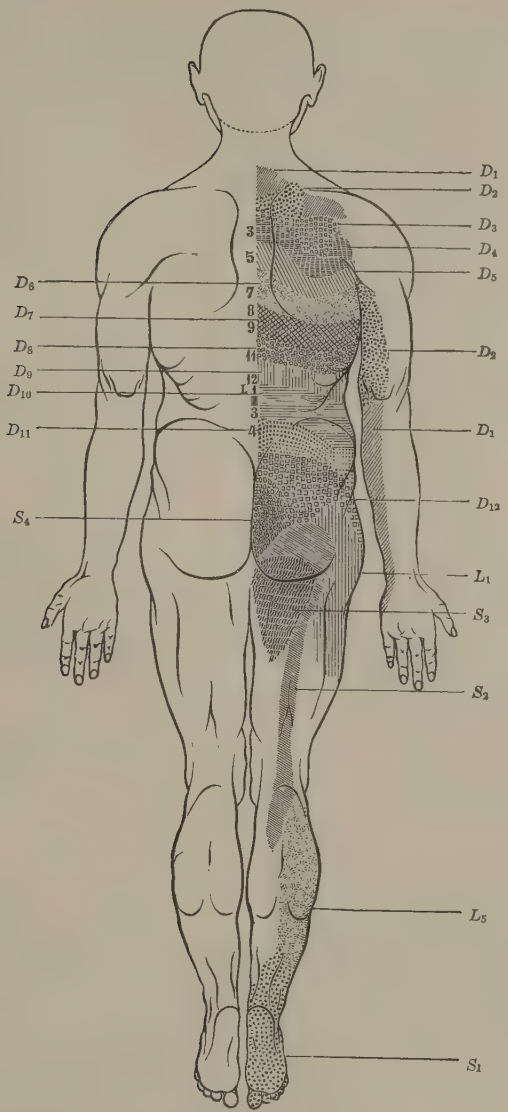


Fig. 382.—Hyperalgesic and radiation zones of the skin in diseases of deeply situated organs. Zones on the trunk and extremities: Diseases of the heart, pain, and hyperesthesia in zones, C_3,[1] D_1, D_4; tuberculosis of the lungs, D_1–D_7, particularly D_2, D_4, D_5; diseases of the esophagus, particularly D_5, D_6, D_8; diseases of the breast, D_4, D_5; diseases of the stomach, D_7, D_8, D_9; diseases of intestine (pylorus, colon), D_{10}, D_{11}, D_{12}; diseases of liver, D_7, D_8, D_9, D_{10}; diseases of the kidney and ureters, D_{10}, D_{11}, L_1; diseases of the bladder, S_2, S_3 S_4; diseases of the ovaries and testicles, D_{10}; diseases of the uterus, D_{10}, D_{11}, D_{12}, L_1; diseases of the cervix, S_1, S_2, S_3, S_4 (after H. Head).

[1] See Fig. 383.

sections for the sensory paths of the corresponding cutaneous surfaces, and thus cause the latter to appear hyperalgesic. In contrast to actual sympathy or irradiation, this radiated stimulation is not strong enough to be appreciated by the sensorium as pain, but is merely sufficient to cause hyperirritability of the sensory conductions coming from the skin.

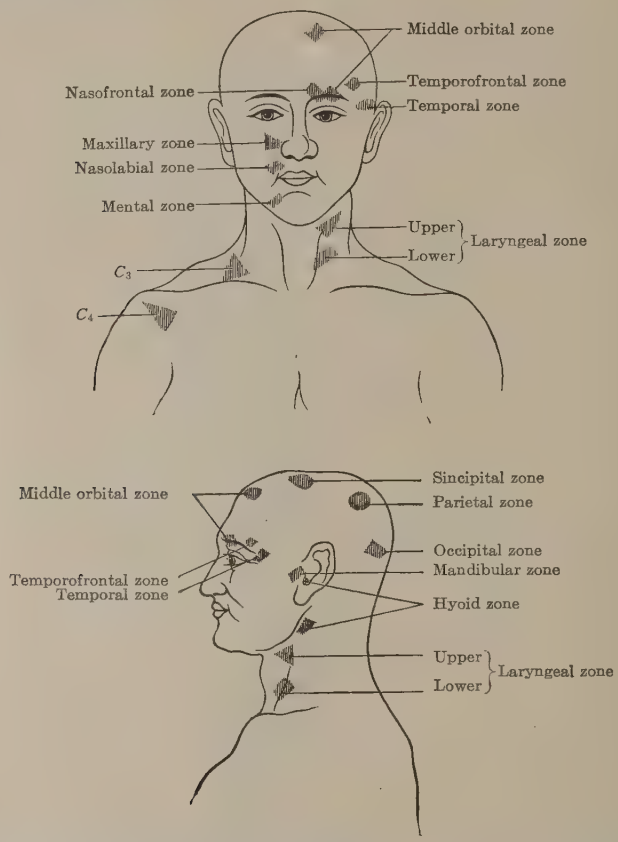


Fig. 383.—Hyperalgesic and radiation zones of the skin in diseases of deeply situated organs. Zones on the head and neck: Nasofrontal zone, diseases of the eyes, nose, and upper incisors; middle orbital zone, in hypermetropia; temporofrontal zone, diseases of the ears and heart; temporal zone, in glaucoma (after H. Head).

Sincipital zone: Diseases of the middle ear.
Parietal zone: Diseases of the ear and stomach.
Occipital zone: Diseases of the posterior half of the larynx and certain abdominal viscera.
Maxillary zone: Diseases of the iris and vitreous body.
Mandibular zone: Diseases of the upper molars.
Nasolabial zone: Diseases of the nose and dental pulp.
Mental zone: Diseases of the incisors and canines.
Hyoid zone: Diseases of the tonsils, tongue, and lower molars.
Upper laryngeal zone: Diseases of the dorsal surface of the tongue and the wisdom teeth.
Lower laryngeal zone: Diseases of larynx.

Fig. 380 explains the process diagrammatically: *a* Represents the diseased organ with a centripetal stimulation proceeding to a sensory station, (*b*) for example, in the spinal cord; from there the stimulation can come to the sensorium (*c*), either directly (*b–c*) or indirectly (*b–d—f*), jumping to a neighboring sensory tract (*e*, *f*). If

this process of irradiation produce a painful stimulation at *d*, a painful sympathetic sensation will be referred to the cutaneous area (*e*); whereas if it produce merely a hyperirritable condition at *d*, the cutaneous area (*e*) will present a hyperalgesia to pressure and to other stimulations not usually causing pain. Thus, circumscribed cutaneous hyperalgesias, if anatomically established, may, under some circumstances, possess the same diagnostic value as actual sympathetic sensations.

Head, of London, has taken pains to investigate these zones of cutaneous hyperalgesia in a great number of pathologic conditions in order to establish some diagnostic relations to deep-lying diseases. Corresponding to the above explanation, he found that the hyperalgesic zones were identical with the zones to which the irradiation pains were projected in the diseased organs in question. He tabulated his observations in the accompanying plates (Figs. 381, 382, and 383). The separate zones are shaded differently. The numbers and letters refer to the segments of the spinal cord (designated according to the corresponding spinal nerves) whose stimulation is the cause of the cutaneous hyperalgesia (based upon our knowledge of the spinal sensibility topography of the skin (see p. 1143 et seq.). Probably the affected organs are also supplied by the same nerves. Thus far no satisfactory anatomic explanation has been able to correlate the localizations of hyperalgesic zones of the head to definite diseases.

Though interesting theoretically, Head's statements need further confirmation and perhaps modifications. Such relations of the deeper organs to the surface of the skin make one appreciate the therapeutic action of counterirritation to the skin, especially upon deep-seated pains. It is only fair to suppose that the same anatomic tracts which conduct the cutaneous hyperesthesias in diseases of the deeper organs can be utilized to transmit inhibition of pain by vigorous stimulation of the skin.

IV. EXAMINATION OF THE REFLEXES[1]

In testing reflexes it is advisable to distract the patient's attention as much as possible from the parts under examination, otherwise an involuntary inhibition may alter the reflex. The simplest device is to direct him to close his eyes. The fatigue of a reflex is sometimes responsible for mistakes in diagnosis. The response to the first tap should be observed attentively, because it may disappear after one or two repetitions. If the first response had not been noticed, the examiner would then incorrectly consider the reflex absent. It is, therefore, a safe rule to observe each reflex quickly and accurately, and to utilize repeated, careful examinations in order to discriminate in any doubtful case, for reflexes, like other nervous functions, often vary at different times. These precautions are especially valuable in testing the patellar reflex, which is so important in diagnosis.

Ordinarily, the reflexes are local in character, *i. e.*, they take place in the region of the body that is irritated. But with an increase in the reflex irritability, which may be partly within the normal physiologic limits and depend partly upon reflex stasis (described upon p. 994), the reflexes may be diffused in cross and longitudinal directions to other muscle areas and to other extremities. This corresponds to Pflüger's laws of reflex dispersion.

Increase of the reflexes, as well as decrease or absence and qualitative abnormalities (the so-called pathologic reflexes), are of considerable importance for diagnosis.

NORMAL CUTANEOUS REFLEXES

The cutaneous reflexes of the upper extremities and of the face are very inconstant. They have, therefore, no diagnostic significance

[1] The reflex belonging to the cranial nerve territory will be described more fully in the special part devoted to examination of the separate cranial nerves. (Concerning the bladder and rectal reflexes, see the section upon Examination of the Bladder and Rectal Functions.)

except when decidedly increased. The following cutaneous reflexes are clinically the most important:

Plantar Reflex.—Tickling or pricking the sole of a healthy person's foot produces a plantar flexion of the toes. (See Fig. 384.) A stronger irritation produces a dorsal flexion of the toes, combined with a dorsal flexion of the foot and flexion of the knee and hip-joints.

The **cremaster reflex** is elicited when the inner surface of the thigh is irritated by scratching or pricking, or by stroking it quickly with the handle of a percussion hammer or some similar object. It consists of a sudden contraction of the cremaster muscle, which draws up the testicle. This reflex should not be confused with the slow, worm-like contraction of the tunica dartos, which frequently follows uncovering the patient, as a result of cooling.

The **inguinal reflex** (oblique reflex) (K. Geigel[1]) can be elicited in both sexes by an irritation similar to that described for the elicitation of the cremaster. It consists of a contraction of the lower fibers of the internal oblique muscle above and along Poupart's ligament. Since the cremaster muscle is nothing but a bundle of the internal oblique passing with the testicle through the inguinal canal, the cremaster reflex in reality belongs to the inguinal reflex. Examination of the latter in the female sex takes the place of that of the cremaster reflex.

The **abdominal reflex** is produced by tickling, scratching, or pricking the skin of the abdomen. It consists in a simultaneous contraction of the transverse oblique and recti muscles of the abdomen, which produces a depression of the abdomen and a pulling of the navel toward the side stimulated. While obtaining the reflex, it is better to divert the patient's attention and have him avoid all voluntary tension of the abdomen.

Several abdominal reflexes may be differentiated upon each side of the abdomen —a superior, median, and inferior. Stroking the abdominal wall in a horizontal direction in the region of the epigastrium, mesogastrium, or hypogastrium causes reflex contractions of the abdominal muscles, which remain localized at approximately the height of the stimulation. If, on the contrary, the entire length of the abdomen be stroked in a vertical direction, the whole half of the abdomen is contracted, and the maximum of the excursion is found at the height of the navel. This is what we ordinarily call the abdominal reflex. With more vigorous irritation, horizontal stroking of the abdomen can produce the general abdominal reflex. Strümpell has called attention to the loss of the abdominal reflex on both sides as an important and early sign of multiple sclerosis, and therefore valuable for differentiating it both from pure spastic spinal paralysis and from functional diseases. Jamin has noted the loss of the abdominal reflex on one side in acute inflammatory abdominal affections, *e. g.*, perityphlitis. The most probable explanation of this phenomenon is that it is the result of the voluntary, instinctive and reflex permanent contraction of those muscles directly over the painful part (muscle on guard).

The **interscapular reflex,** which is elicited by stroking the inner edge of the scapula, consists in an adduction of the shoulder-blade. It is frequently absent.

The **gluteal reflex,** a contraction of the gluteal muscles produced by an irritation of the skin about the gluteal region, is also inconstant.

Anal Reflex.—Irritation of the skin of the anus, as by a pinprick, elicits a contraction of the external sphincter. It is often absent. (Consult p. 995 et seq. and p. 1151 et seq. in regard to the diagnostic significance of abnormalities of the cutaneous reflexes and their localization in the spinal cord segments.)

[1] Deut. med. Woch., 1892, vol. viii, p. 166.

NORMAL TENDON, PERIOSTEAL, AND JOINT REFLEXES

The **patellar reflex,** or the "knee phenomenon," consists in a contraction of the quadriceps extensor excited by a blow upon the patellar tendon. We may employ the ulnar edge of the hand or, better, the edge of a firm, not too light object, *e. g.*, a percussion hammer.

The **Achilles-tendon reflex** consists in a contraction of the calf muscles excited by a blow upon the Achilles tendon. Another method of exciting this reflex is to increase suddenly the tension of these muscles by a passive dorsal flexion of the foot. If the reflex be increased, the latter method causes a series of rapidly succeeding plantar flexions of the foot, which often persist as long as dorsally directed pressure is exerted upon the ball of the foot. The repetition of the flexions apparently depends upon the fact that each contraction of the calf muscles temporarily removes the pressure upon the plantar surface, so that the pressure acts later as a renewed blow. We call such an increase of the Achilles-tendon reflex "the foot phenomenon," "foot-clonus," or "ankle-clonus."

The **tendon reflexes** of the upper extremities are rather inconstant. In healthy individuals a flexion of the hand can sometimes be obtained by striking the flexor tendons at the wrist-joint, a bending of the forearm from the biceps tendons, or an extension from the triceps tendons. If the reflexes be increased, a similar result can be obtained, even in the upper extremities, by striking almost any of the tendons. Sometimes an actual clonus can be produced by vigorously flexing the hand dorsally, "hand-clonus" (analogous to ankle-clonus).

Periosteal and **joint reflexes** are produced by striking various bony prominences and joints. They are inconstant in health. The best-known periosteal reflexes are those of the ulna and the radius at the wrist-joint. On testing the latter, flexion and pronation of the hand and flexion of the fingers usually appear.

In testing tendon and periosteal reflexes it is especially important to observe the caution enjoined above, that is, to distract the attention of the patient from the part of the body to be examined, since otherwise, through involuntary tension of the muscles in question, the reflex may be inhibited. A very good plan is to interest the patient in some subject, and to engage him in conversation while you are testing. Jendrassik's device for reinforcement is often very successful in testing the tendon reflexes of the lower extremities. The patient is directed to lock his fingers and pull strongly, as if tearing them apart, but without separating them. Not infrequently, however, this reinforcement does the opposite to what it usually accomplishes, *i. e.*, it weakens or inhibits the patellar reflex, probably because, instead of actually concentrating his entire attention and effort upon the fingers, the patient renders the muscles of his lower extremities tense by associated movement, and so inhibits the patellar reflex. Another precaution that should always be taken is to be sure that the muscles concerned in the reflex are actively relaxed, but passively tense. This is especially important in testing the patellar reflex. For the latter, the sitting posture is most desirable, with the leg to be examined crossed and hanging limply over the other. In bed-ridden patients the leg is supported below the knee by the hand of the examiner in semiflexion.

CONSTANCY (*i. e.*, FREQUENCY) OF OCCURRENCE OF THE NORMAL SPINAL REFLEXES

Of the above-described reflexes, there are only a few which are fairly constant, and even these not absolutely. Some are even present only in a minority of cases. According to the researches of Pflasterer,[1] the reflexes are found as follows:

MALES

Epigastric reflex (upper abdominal wall reflex)	present in 62 per cent.[2]
Abdominal reflex (middle abdominal wall reflex)	" " 99 "
Cremaster reflex	" " 66 "
Plantar reflex	" " 98 "
Interscapular reflex	" " 15 "
Gluteal reflex	" " 28 "
Periosteal reflex of the anterior tibial edge	" " 5 "
Periosteal reflex of the lower end of the bones of the forearm	" " 29 "
Patellar reflex	" " 98 "
Achilles tendon reflex	" " 57 "
Biceps tendon reflex	" " 47 "
Triceps tendon reflex	" " 48 "

FEMALES

	Present.	Absent.	Unilateral.	Doubtful.
Plantar reflex	88	11	1	
Abdominal reflex	92	7		1
Interscapular reflex	13	86	1	
Gluteal reflex	11	89		

The foregoing shows that the absence of the reflexes printed in italics only is of diagnostic value.

RECENT VIEWS CONCERNING THE PHYSIOLOGIC ORIGIN OF THE REFLEXES AND THEIR ALTERATION IN PATHOLOGIC STATES.—BLOCKING OF THE REFLEXES

Formerly it was believed that the spinal cord was the center of all reflexes. This view was based upon the results of animal experiments and upon the observation that most transverse lesions of the cord were associated with increase of the reflexes. Modern neuropathologists, however, following the teaching of Bastian, endeavor to dethrone the cord from its position as a reflex organ in man. Bastian and others have shown that all the reflexes were found to be completely abolished in some cases in which there is complete transverse lesion of the spinal cord. It was, therefore, argued that no transverse lesion could be complete if the reflexes in the region innervated below the injury either persisted or were increased. A few such observations, however, proved nothing, because the part of the spinal cord situated below the obstruction might be affected in such cases by inhibition or by a diminished blood-supply conditioned by lesion of the spinal arteries.[3] In order to determine whether the reflexes of clinical importance have their centers in the spinal cord, it is much more essential to inquire whether there have been cases with persistent reflexes of the lower extremities in which a careful anatomic examination has shown postmortem complete cross-section of the spinal cord. In recent years such cases, absolutely free from question, have been described,[4] and show, beyond doubt, that the

[1] Cited by K. Geigel, Deut. med. Woch., 1892, No. 8, p. 166.

[2] The author regards this as too low.

[3] Gerhardt, Ueber das Verhalten der Reflexe bei Querdurchtrennung des Rückenmarkes, Deut. Zeit. f. Nervenheilk., 1895, vol. vi, p. 127, and Jendrassik, Ueber die allgemeine Localization der Reflexe, Deut. Arch. f. klin. Med., 1894, vol. lii. [4] Ibid.

tendon reflexes, at least, are independent of nervous mechanism beyond the spinal cord. Similar results have been proved by the persistence of the tendon reflexes after decapitation (Laborde).[1] Hence it is plainly incorrect to maintain that all reflexes require the aid of the brain.[2] The discussion has been valuable in more accurately determining the merits of the earlier conception, which argued that all reflexes took place in the spinal cord and homologous portions of the brain stem. In this connection Jendrassik has formulated a theory of the reflexes which is based upon clinical evidence and which is worthy of careful study. [See also upon this subject, Collins and Fränkel, Muscle Tonus and Tendon Phenomena, Medical Record, December 12, 1903.—Ed.]

According to Jendrassik, there are spinal and cerebral reflexes, as well as a combination of the two, *i. e.*, reflexes requiring both cerebral and spinal center for their normal occurrence. He subdivided the physiologic reflexes and characterizes them as follows:

I. **Spinal Reflexes.**—This division includes *tendon, periosteal*, and *joint reflexes*. Their characteristics are as follows: 1. They are generally discharged from parts which possess little sensation. 2. The reflex is associated with no particular feeling. 3. The discharge takes place by means of a simple mechanical irritation, such as a blow, etc. 4. The intensity of the reflex depends upon the degree and not upon the duration of the irritation. 5. The reflexes are quite as easily excited in ourselves as in others. 6. The latent time of the reflex, corresponding to its origin in the spinal cord, is the shortest. 7. The ensuing movement is a very simple one, and serves a recognizable purpose. 8. Making other muscles tense increases the reflex (reinforcement method of Jendrassik; see, however, p. 989). 9. Delay of these reflexes never occurs pathologically. 10. Psychic influences have no effect upon these reflexes aside from distraction of attention, which increases them.[3]

II. **Cerebral Reflexes.**—These are, to a large extent, the cutaneous reflexes. The scapular, abdominal, cremaster, gluteal, plantar, eyelid, palatal, conjunctival, and anal reflexes belong to this group. Their characteristics are as follows: 1. They are discharged from sensitive spots which are not ordinarily accustomed to a light touch (tickling). 2. The liberation is associated with a specific sensation (prickings, cold, tickling, etc.). 3. Brief stimulation is efficacious for their liberation, just as it is for the spinal reflexes described in the previous paragraph. 4. A light touch has often a more vigorous action than a stronger one; individuality has a decided influence. 5. These reflexes can scarcely ever be liberated by the person himself, and then only very slightly. 6. The latent time is longer and not so constant as with the spinal reflexes. It is quite dependent upon the sensation time and corresponds to the reaction time, *i. e.*, the time which the voluntary reaction demands of a sensory stimulation. 7. The resulting movement is simple, and its principal characteristic is that it shows an effort to escape from the irritation. 8. Increased activity of the other muscles never increases the reflex, but may even diminish it. 9. These reflexes are diminished on the paralyzed side in cerebral hemiplegia. 10. They are delayed in cases of delayed sensation. 11. Psychic influences can either diminish or increase these reflexes; distraction of the attention impairs them.

III. **Complex Reflexes.**—To this group belong reflexes which have complicated "centers" within which the reflex occurs, not as a single movement, but as a series of such, *e. g.*, sneezing, vomiting, swallowing, coughing, urinating, defecating, genital reflex (ejaculation). The characteristics in common are as follows: 1. They are liberated from very sensitive places. 2. The liberation takes place with a specific sensation which plays even a greater rôle in the origin of the reflex than in those of the cerebral group. 3. The liberation requires protracted stimulation. 4. Individuality has a great influence upon the occurrence of the reflexes. 5. The stimulation which produces these reflexes is a specific and complicated one. 6. The

[1] Quoted by Jendrassik.

[2] According to Bastian's and Jackson's view, especially of the cerebellum. The author believes that the cerebrum is still more essential.

[3] The author has found that psychic excitement considerably increases tendon reflexes and this increase may serve as an important sign of states of psychic excitement.

latent time is longer than for any of the other reflexes. Their liberation seems to require a sort of summation of stimuli. 7. The resulting movement is very complicated and bilateral; several muscle groups take part, and in some of them the reflexes act antagonistically. 8. Muscular activity weakens their effect to some extent. 9. Psychic influences produce a great effect. 10. Reflexes of this group belong to the vegetative functions.

The distinction between Groups III and II is essentially this: in the latter the sensation is transposed directly into simple reflex movements; whereas in the former, the sensation, *i. e.*, the cortical stimulation, first of all excites a complicated reflex center of activity. This center is composed of several distinct centers, and within the main center the reflex process then takes an independent course. Should this subdivision be accepted, the author would call attention to the fact that the peculiarities stated by Jendrassik as characteristic of the individual groups do not always materialize. It would lead us too far, however, to discuss these points in detail. For the last group of Jendrassik the author would suggest the name of corticonuclear reflexes. Those which also involve spinal areas of innervation might with equal propriety be designated as cerebrospinal reflexes. In the individual corticonuclear reflexes the cerebral factor plays a varying but important part, as is shown by the fact that completely unconscious individuals never cough nor sneeze, but, on the other hand, they can, under some circumstances, still swallow and urinate and defecate normally, even if unwittingly.

Various examples might be added to show how dependent the reflexes of Groups II and III are upon the cerebrum; but the author will allude only to the following: the diminution of the cutaneous reflexes over the anesthetic area of the hysteric; the purely cerebral origin of the plantar reflex in ticklish persons, in whom it may be elicited by threatening to tickle them, even without touching them; and the occurrence of vomiting evoked by some disgusting conception.

Recognizing the above theories of the origin of reflexes, we should now attempt to explain their clinical manifestations under pathologic conditions, especially in the case of an interrupting focal lesion of the brain and spinal cord.

Cerebral Hemiplegias.—The tendon reflexes are here, as a rule, preserved, because they come under Group I (the spinal). In the beginning they may be lost, presumably on account of the inhibiting action of the lesion, but later they are usually increased, because of the complete abolition of cerebral inhibition. (See p. 952 et seq., Active Contractures.) The behavior of the cutaneous reflexes (Group II) in cerebral hemiplegia is explained by the supposition that the voluntary tracts (pyramidal tracts) are identical with the motor limb of the cortical reflex arc. We therefore generally find upon the paralyzed side diminution or disappearance of the cutaneous reflexes (p. 991, Group II), because its reflex arc is interrupted. In hemiplegia of indirect origin, *i. e.*, when the lesion is not immediately of the pyramidal tract, the cutaneous reflexes may be retained, although they, too, are in the beginning usually diminished. This is explained by the supposition that the lesion here does not permit the passage of the voluntary impulse, while it offers no obstacle to the reflex impulse. The persistence of the cutaneous reflexes upon the hemiplegic side can be regarded as a favorable prognostic sign, because it argues for an incomplete interruption of the motor tract. The behavior of the complicated reflexes (Group III) in cerebral hemiplegia depends upon the varying degree of influence which the cerebral factor has upon their origin. As a general rule, they are not affected, because they are bilaterally innervated.

Transverse Lesions of the Spinal Cord.—If Jendrassik's conception be correct, the tendon reflexes must in general be considered pure spinal reflexes, and the cutaneous, on the other hand, cerebral reflexes. Clinical experience does not seem to coincide perfectly with this conception, for we ordinarily find both the cutaneous and the tendon reflexes increased in transverse spinal cord lesions, such as those caused by myelitis. How is this to be explained. The persistence of the tendon reflexes is clear enough, and their increase is easily explained by supposing that the inhibitory fibers running in the affected pyramidal tracts have been cut off; but how can we explain the increase of the cutaneous reflexes, if, as Jendrassik assumes, they really have their reflex arc in the brain? Jendrassik considers that these reflexes, which in transverse cord lesions are ordinarily regarded merely as accentuated cutaneous reflexes, are in reality pathologic cutaneous reflexes, which normally do not occur in this shape at all, but in transverse lesions take the place of the normal cutaneous reflexes which have been destroyed. He offers the following arguments in support of this theory. The normal cutaneous reflexes of the lower extremities can be elicited only from the sole of the foot, no matter how vigorous the stimulation may be; while the pathologic cutaneous reflexes in cross-

lesions of the cord can be elicited by irritating almost any part of the lower extremities. The normal plantar reflex depends upon a sensation of pain and tickling, and the time of its appearance upon the occurrence of such sensations (best recognized in the delayed transmission of pain in tabes dorsalis); the pathologic reflexes, on the contrary, are neither connected with nor dependent upon sensation. The physiologic reflex exhausts after repeated testing, even though it is very vigorous; whereas the pathologic reflex never exhausts; it can be elicited again and again. A light touch will very easily stimulate the physiologic cutaneous reflex; whereas the pathologic reflex is in direct ratio to the intensity of the irritation. The pathologic cutaneous reflex of the lower extremity always consists of a maximum flexion of the thigh, outward rotation of the knee, and the dorsal flexion of the foot (in rare instances the reverse, *i. e.*, an extension of the thigh and plantar flexion of the foot). Both of these types are very different from the physiologic reflex, which is essentially a movement of escape, and consists of a plantar flexion of the toes and a dorsal flexion of the foot, accompanied by a very slight movement of the muscles of the thigh and pelvis. Jendrassik explains the appearance of these vigorous abnormal reflexes of transverse cord lesions in the place of the normal by assuming that the sensory impulses which are cut off at this point of the lesion make for themselves a sort of lateral path which is not normally in use. There are cases of acute transverse lesions of the cord in which the cutaneous reflexes are diminished instead of increased. In them he assumes that the lower part of the spinal cord is also affected, so that these pathologic reflexes cannot take place perhaps because of an anatomic lesion (deficient blood-supply), or perhaps on account of an inhibitory influence by the lesion. A similar explanation will account for the loss of the tendon reflexes which we see so often in acute traumatic complete transverse division of the cord. The increase of the tendon reflexes, and the appearance of the pathologic cutaneous reflexes which is observed later in the course of these cases, are sufficient evidence to support such an explanation.

Jendrassik's theory of the genesis of the reflexes has many arguments in its favor, but in the author's opinion is very weak in one point—the supposition that in transverse lesions of the cord the reflexes which belong to parts supplied by the lower portion of the cord are not the ordinary retained reflexes, but pathologic reflexes of newly opened pathways. This assumption seems permissible in the case of the vigorous and altered reflexes of the lower extremities, as they were described above. But should the cremaster and abdominal reflexes, etc., be preserved in a myelitis of the upper dorsal cord with complete motor and sensory paralysis, it compels us to assume that such circumscribed reflexes must arise by a path other than the physiologic, and that in such complete paralysis the physiologic cerebral reflex is cut off. The persistence of these reflexes, whether weakened, normal, or increased (any one of these conditions is possible in transverse lesions), is most readily explained by assuming that their center or, better expressed, their reflex arc lies below the transverse lesion, and is thus preserved. On the other hand, the absence of these reflexes in cerebral hemiplegias seems difficult to reconcile with such a supposition. The following theory will, the writer believes, clear up the difficulty: The cutaneous reflexes which Jendrassik considers to be purely cerebral are in reality like his third group (p. 991), corticonuclear, *i. e.*, cerebrospinal in so far as they belong to spinal areas. They have a reflex center or, better,[1] a lower short reflex arc in the cord, and, furthermore, a more highly differentiated "upper" reflex arc in the brain. In a sense they possess two collateral reflex arcs. (See Fig. 464, p. 1151.) Under ordinary circumstances an accompanying excitation of the cerebral arc is essen-

[1] Compare p. 1151 et seq., Segmental Localization. The expression "reflex center," employed merely for the sake of brevity, is inaccurate and incorrect, and the conception according to which it was first used is no longer tenable.

tial to the operation of the reflexes. This arc, when so stimulated, transmits a centrifugal impulse to the spinal reflexes. In a motor hemiplegia of cerebral origin the lesion (*a b*, Fig. 464) interrupts the centrifugal tract from the brain to the spinal reflex center (this tract is either identical with or situated very near to the pyramidal tract). Hence the cutaneous reflexes upon the paralyzed side disappear. In a transverse lesion of the cord (*c d*, Fig. 464) the cerebral reflex arc is also interrupted, and one would naturally expect a similar disappearance of the cutaneous reflexes; but this does not occur, because the lesion, by interrupting the sensory conduction in the cord, in a measure dams the sensory stimulation. Therefore, the peripheral impulse must find a path in the region of the lower cord segments. It generally selects the customary path, *i. e.*, the formed spinal reflex arc of the corresponding cerebrospinal reflex, and so the cutaneous reflexes become purely spinal.

This explains how many of the preserved reflexes, *e. g.*, the abdominal cremaster, retain their complete physiologic distribution. It also explains how other reflexes, by means of the damming up of exciting impulses at the lesion, attain both abnormal intensity and distribution by transmission of the impulse to neighboring paths. (Jendrassik's Pathologic Reflexes, see p. 997 et seq.)

The stasis of the excitation at the level of the lesion is sufficient to account for the abnormal intensity of the reflexes in transverse lesions, even without the assumption of abolition of the reflex inhibitory tracts (although the latter shall not be contested).

On the other hand, in cerebral hemiplegia, since extensive by-paths in the whole cord and a great part of the brain are open to centripetal excitation (Fig. 464, lesion *a b*), there is no reason for an actual stasis, and likewise no ground for assuming a pure spinal origin of reflexes which otherwise come from the brain. These, therefore, from lack of cerebral excitation, disappear, or, through insufficient exertion, appear weak. Perhaps we can assume that the centripetal impulses here are dispersed so completely through the wide-open tracts of the nervous system that they become inert and run, like a lightning-rod, into the ground. The author can claim more than a mere diagrammatic representation for this theory of damming back and jumping over of sensory irritation in the cord, because Golgi has demonstrated the existence of branched sensory collaterals (Fig. 464), and has shown that paths for discharge are open upon all sides, and that it depends only upon the intensity of the resistance which of these pathways will be selected by the stimulation, *i. e.*, the reflex. The diminution of the reflexes sometimes observed in very acute, especially traumatic, cord affections is, according to this theory, to be attributed to inhibition or to injury of the lower cord segments from circulatory disturbances, etc. The behavior of the function of the bladder and rectum according to this conception will be discussed later. (See p. 1162.)

The author's theory, contrasted with Jendrassik's, simplifies the scheme of the reflexes. We should differentiate physiologically between only two groups of reflexes. The first group would comprise *purely spinal* or, better, *purely nuclear* reflexes, because some of them occupy the region of the cranial nerves, and would include the tendon, periosteal, and joint reflexes. The second group, the cerebrospinal, *i. e.*, cerebronuclear, reflexes, would include both the normal, simple, cuta-

neous, and mucous membrane reflexes and the complicated reflexes of Jendrassik's third group—bladder, rectal reflexes, etc. In the second group the brain and spinal cord (or the cerebral cortex and cranial nerve nuclei) act normally together, *i. e.*, the activity in a lower (nuclear) reflex arc is, under physiologic conditions, discharged by the cortex. In transverse lesions of the cord, reflexes of this second group may be originated exclusively by way of the spine, and so be increased or even deformed by reflex damming. This conception seems to the author the only one which corresponds to our clinical experience. That of Jendrassik is essentially opposed to the facts, inasmuch as it does not recognize the short spinal path for normal cutaneous reflexes which has been localized by pathologic and experimental findings (see Table upon p. 1153 et seq.), and which is made use of for the purpose of local diagnosis. Their existence is shown by the occurrence of undeformed reflexes in total transverse lesions of the spinal cord.

DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF QUANTITATIVE ALTERATIONS OF THE REFLEXES

The demonstration of the presence of a reflex is of greater diagnostic significance than the demonstration of its absence or diminution, because its presence is conclusive evidence of an intact reflex arc; whereas, although its absence or diminution may mean that the arc is interrupted, it may also mean that the reflex is affected by a mere inhibition or by remote influence from some circulatory disturbance. Similarly, an increase of a reflex is ambiguous. The latter may be caused by lesions which directly stimulate the reflex centers or tracts, or by those which remove inhibition or injure inhibitory tracts. The pathologic relations of the reflexes are, therefore, evidently complicated. Only a comparatively few types will be mentioned.

The relation of altered reflexes to lesions which are situated in the lower (nuclear) reflex arcs is perhaps the most distinct. (See p. 995 et seq., and Fig. 464.) Any such lesion, whether of the sensory limb, nucleus, or motor limb, is capable of diminishing or destroying the reflexes. Such reflexes as the cutaneous, which are partly cortical, and which possess both lower and upper reflex arcs, require integrity of the lower reflex arc for the proper display of the reflex, because, according to the author's idea, the upper reflex arc has no functional independence, but merely incites the lower reflex arc to activity. So anatomic lesions of its nuclear arc cause a diminution or disappearance of that reflex. The disappearance of the tendon reflexes in tabes, and the disappearance of all the reflexes in peripheral neuritis and other peripheral paralyses, are examples in point. On the other hand, an accentuation of the reflexes results from an increase of irritability in the lower reflex arc, *e. g.*, in tetanus, in hysteric and neurasthenic states, and occasionally in the beginning stages of neuritis, especially while associated with hyperalgesia. The last may sometimes occasion difficulty in diagnosis.

The reflexes in cerebral hemiplegias and in transverse lesions of the cord have been so fully discussed in the preceding section (p. 992 et seq.) that only a few diagnostic points need be added. Cerebral hemiplegias can sometimes be diagnosed by the diminution of the cutaneous reflexes, and the alterations of the tendon reflexes (increase or decrease)

upon the paralyzed side, even during the "stroke," when the patient is still unconscious, and while, therefore, the motility cannot be directly tested. The abdominal reflexes, particularly the cremaster in men and the crural in women, are especially significant, unless these reflexes are absent upon both sides on account of inhibitory influences. In the latter event the criterion fails, and the condition is evidently more serious. Preservation of the cutaneous reflexes upon the paralyzed side should always be considered a relatively favorable prognostic sign, because it shows that the upper reflex arc through the cerebrum, whose motor limb is practically identical with the voluntary motor tract, has not been entirely destroyed. (See p. 992.)

In transverse lesions of the cord we generally find an accentuation of the reflexes whose nuclear arc lies below the injury. A decided increase of the cutaneous reflexes, *i. e.*, the appearance of pathologic skin reflexes, implies a serious lesion. On the other hand, a decided diminution of the reflexes originating beneath the lesion shows either that an inhibitory influence proceeds from the injury or that there exists a coincident involvement of the spinal segment situated below the lesion. Such an involvement may be the result of circulatory disturbance or of a distinct longitudinal lesion of the cord. Bastian, Kocher, and others consider that a traumatic lesion which causes a disappearance of the tendon reflexes of the lower part of the body is probably complete. The author's theory would attribute this to a decided inhibitory action in the lower segment, and perhaps also to a circulatory impairment from a lesion of the spinal arteries or other disturbances of circulation. At all events, later in the course of these cases, although the continuity of the cord is not reëstablished, the tendon reflexes sometimes reappear. Our discussion upon the causes of the accentuation and variation of the cutaneous reflexes depending upon transverse lesions presents an important consideration for the operative treatment of spinal cord compression (spondylitis, etc.), viz., the nearer the reflex approaches to the normal, the more liable the cord is to be merely compressed and otherwise intact. Again, the more profound and extensive the cross-lesion, the more pronounced will be the signs of what we have called reflex damming. In other words, decided accentuation or variation or loss of the reflexes argues in favor of a serious focal lesion and against simple compression. The preservation of certain reflexes is very important in cross-lesions, because it enables us to localize the level and the extent of the lesion (p. 1151 et seq.). The loss of them is, as we have seen, less serviceable for localizing diagnosis, because of so many indirect influences which can affect them.

In spastic paralyses it is very difficult to make any diagnostic use of certain reflexes. If the paralyzed muscles be rigidly contracted, neither cutaneous nor tendon reflexes can be sufficiently manifest in the very tense muscles. Sometimes this is especially noticeable in tetanus, where the permanent tension of the muscles prevents the ordinary reflexes, and yet the appearance of jerks at any irritation leads us to conclude that there is an accentuation of the reflexes.

The behavior of the vesical and rectal reflexes will be specially considered on p. 1162 et seq.

The influence of toxins on the reflexes has been recently studied. Schultze observed the Argyll-Robertson phenomenon in pneumonia, and a number of

writers[1] have frequently found the patellar reflex lost either on one or both sides in this disease. This illustrates the importance of the influence of toxins in the origin of tabes dorsalis.

QUALITATIVE ALTERATIONS OF THE REFLEXES; PATHOLOGIC REFLEXES

Many so-called pathologic reflexes should be regarded, from what was said upon p. 993, as deformations of the normal reflex, depending upon an encroachment of the reflex impulse upon pathways which become accessible to the impulse only because an obstruction is intercalated in the ordinary reflex tract in consequence of reflex damming. Frequently by this procedure the original reflex is only modified, so that, although disfigured, we can still recognize it. In other cases, however, reflexes occur, in quite an analogous way, entirely as pathologic phenomena. It is impossible to enumerate here all those which are observed in transverse lesions of the spinal cord; but there is a pathologic plantar reflex which is so frequently observed in such lesions that it deserves a brief notice. Stimulation of the sole of the foot, without producing plantar flexion of the toes and sometimes even without producing dorsal flexion of the ankle-joint, causes an exaggerated flexion of the thigh, often combined with external rotation. Not infrequently such movements are combined with reflex movements of quite distant muscle territories, *e. g.*, of the abdomen, of the opposite leg, and of the arms. This pathologic reflex can frequently be elicited by irritating other parts of the extremity, such as the thigh.

Babinski's phenomenon or the **Babinski reflex** (**phenomen des orteils**) consists of a dorsal flexion of the toes, but more especially of the great toe [and a simultaneous plantar flexion of the other toes.—Ed.], when the sole of the foot is irritated by pricking or stroking with a moderately sharp instrument. This reflex comes under the head of the pathologic plantar reflexes, and is sharply contrasted with the normal plantar flexion of all the toes on irritation of the sole of the foot. Babinski found that this reflex depended nearly always upon a lesion of the pyramidal tract. H. Schneider,[2] and many other writers [especially Walton and Paul, Journal of Nervous and Mental Diseases, 1903.—Ed.] have confirmed Babinski's original observation. Schneider explains this reflex as follows: In the ordinary reflex of the sole of the foot the, plantar flexion of all the toes depends upon a cortical component of the reflex; whereas the dorsal flexion depends upon a medullary component of the reflex. With a lesion of the pyramidal tract, the reflex for the plantar flexion is interrupted, but not that for the dorsal flexion. Babinski's reflex may also be produced by an increase of the medullary component of the reflex, just as well as by a lesion of the pyramidal tract; therefore, its demonstration does not prove absolutely a lesion of the pyramidal tract. It seems to the author, however, that the hypothesis of deformations of the reflexes by damming, which he has advanced, will explain the transformation of the usual plantar reflex into Babinski's reflex quite as well as Schneider's hypothesis. Babinski's reflex may be obtained more readily by stroking the outer than the inner plantar margin. In fact, several cases have been reported in which a Babinski reflex could be elicited from the outer margin, and a plantar flexion of the toes from the inner margin, of the sole of the foot. A plantar reflex of the Babinski type may be produced if, in a nuclear lesion of the lumbar cord or in a peripheral palsy of the lower extremities, the flexors of the toes are paralyzed, either alone or in a greater degree than the extensors. In this case the reflex impulse in the extensors preponderates. Physiologically, the Babinski reflex appears in sleep, at the commencement of narcosis, and during the first year of infancy.

Oppenheim's dorsotibial phenomenon is analogous to Babinski's sign; and, like the latter, is capable of different explanations in isolated cases. It consists of a dorsal flexion of the foot and toes when the inner surface of the leg is stroked, whereas under ordinary circumstances either no reflex at all or a plantar flexion of the toes and foot would result.

K. Mendel[3] has described an additional pathologic "dorsum foot-reflex," which was also described by von Bechterew, and is sometimes called Bechterew's "flexor reflex." According to Mendel, if one tap the dorsum of the foot of healthy indi-

[1] Marinian, Rivista Clinica, Bologna, 1884; Longard, Zeit. f. Nervenheilk., 1891; Luethje, v., Münch. med. Woch., 1902, No. 32; Burnes, Birmingham Med. Review, April, 1907; and Wiens, Zeit. f. klin. Med., 1908, vol. lxv, p. 53.

[2] Literature in von Kornilow's article, Zeit. f. Nervenheilk., vol. xxiii, p. 304; Richter, Münch. med. Woch., 1903, No. 24; Berlin. klin. Woch., 1901, No. 37.

[3] Neurol. Centralbl., 1904, p. 5.

viduals or those suffering from functional diseases, there will either be no reflex at all or a dorsal flexion of the second to the fifth toes inclusive. In certain organic diseases, however, there is a plantar flexion. According to Mendel, this anomaly is usually but not always combined with Babinski's sign. Very recently L. Jacobsohn [1] has described a reflex of the hand analogous to the Babinski reflex, which, according to him, is constantly found in cases of cerebral spastic paralysis of the upper extremities. He describes the reflex as follows: The patient rests his forearm upon the examiner's hand, with the thumb directed upward, the fingers slightly extended. A blow is then struck with a percussion hammer upon the lower end of the radius on the extensor side. If a flexion of the fingers, especially of the distal ends, results, cerebral spastic paralysis is suggested. Normally, the fingers remain extended.

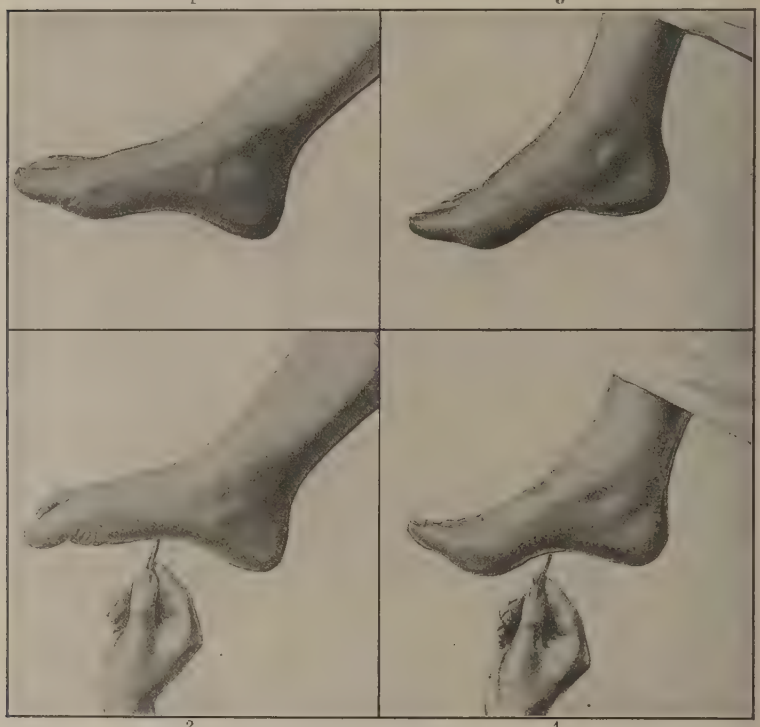


Fig. 384.—Plantar reflex: 1, Foot at rest; 2, plantar flexion (normal); 3, foot at rest; 4, dorsal flexion of great toe (Babinski's reflex).

About the same time von Bechterew also described this reflex and established its analogy to the Babinski reflex. This, however, is obviously a periosteal reflex, while the Babinski reflex is purely cutaneous. Furthermore (see the previous discussion of the Mechanism of Reflexes), our conception of the cutaneous reflex differs in principle from the periosteal or tendon reflexes. As a matter of fact, probably every attentive observer has seen this reflex appear in the contracted upper extremities of hemiplegics, and has considered it in the light of a simple increase of tendon and periosteal reflexes. The deformation in the Babinski reflex, on the other hand, is a normal cutaneous reflex appearing in another form. This does not, at all events, alter the fact that Jacobsohn's reflex as well as the Babinski reflex and, in fact, all exaggerated periosteal and tendon reflexes are important indications

[1] Deut. med Woch., 1908, No. 46.

of lesion of the central neuron. They have always been considered as such, even without the apparently not quite justifiable analogy to the Babinski reflex.

In transverse lesions of the spinal cord the frequent occurrence of ejaculation and erection reflexes, excited by light stroking of the genital or anal region, of the perineum or of the thigh, should be mentioned, as well as bladder and rectal emptying from touching a bed-sore, etc. The testicle reflex described by Kocher in spinal-cord affections consists in a lateral bending of the spinal cord toward the irritated side when the testicle is firmly pinched. The author can confirm the appearance of this reflex in transverse lesions of the spinal cord. Whether it should be considered as pathologic is not easy to determine, because the attempt in healthy individuals, *i. e.*, those with normal sensibility, is very painful and possibly injurious.

Other abnormal reflexes may occur both from cutaneous and from tendon reflexes without assuming damming, but simply from increase of reflex irritability. In this way the impulse can no longer be limited within the stimulated territory, but diffuses itself, according to Pflüger's laws, in horizontal and then in longitudinal directions (p. 988). These phenomena really belong to the section upon Quantitative Alterations.

V. EXAMINATION FOR TROPHIC DISTURBANCES

1. TROPHIC DISTURBANCES OF THE MUSCLES

(*a*) Increase in Volume of the Muscles; Hypertrophy and Pseudohypertrophy

True hypertrophy of the muscles, *i. e.*, an enlargement with increased strength, is a very rare pathologic condition. It occurs, however, in Thomsen's disease and in true congenital muscular hypertrophies. The latter are rarely observed, and still very imperfectly understood. In most cases the pathologic increase in volume of the muscles is not an actual hypertrophy, but a pseudohypertrophy, since it depends not upon an increase of the contracting muscular fiber, but upon a growth of interstitial connective tissue and of fat. The variety of muscular atrophy known as pseudohypertrophic progressive muscular atrophy furnishes the best example of this pseudohypertrophy. Now and then other myopathic forms of chronic progressive muscular atrophy show pseudohypertrophy in some of the affected muscles.

(*b*) Decrease in Volume of the Muscles; Muscular Atrophy

Atrophy of Disuse; Simple Non-degenerative Atrophy.—This means a diminution of the contractile substance which goes on in every muscle that is not used. An absolute increase of interstitial connective tissue does not accompany it, and for this reason this type is designated as a non-degenerative atrophy. Paralysis, mechanical fixation of an extremity, or a restrained position of the latter from some painful affection may gradually produce an atrophy of disuse. This atrophy becomes pronounced only when the immobility is quite absolute. The differentiation of atrophy of disuse from degenerative atrophy is easy without the aid of electric examination, because the volume of that part of the body which shows the atrophy and which is no longer moved is diminished *in toto;* while in degenerative atrophy frequently individual muscles or groups are spared or are predominantly involved in the atrophy.

The above rule, that an atrophy of disuse which depends upon partial inaction of the muscles never attains a very high degree, does not hold good in the case of paralysis appearing in a growing individual. The physiologic growth then seems to be decidedly inhibited by the

inaction, even if very limited, *e. g.*, we frequently observe very marked atrophies in the cerebral paralysis of children, and we can usually definitely determine that these are not degenerative, by means of the anatomic localization of the primary lesion and by electric and anatomic examination of the muscles. It should, nevertheless, be remembered that some of the marked atrophies consequent upon cerebral paralysis in children are possibly also of a degenerative nature, and are brought about in the manner indicated in foot-note 2, on p. 1001.

Degenerative Atrophy.—Degenerative muscular atrophies are distinguished from atrophies of disuse by the presence, in the affected muscles, of a pathologic proliferation of interstitial connective tissue, which develops as well in those idiopathic muscular atrophies called progressive as in the so-called atrophic paralyses.

Progressive Muscular Atrophies.—These include *myopathic, neuritic,* and *spinal* (better nuclear) forms, depending upon whether the muscles are primarily diseased or whether they atrophy secondarily to a chronic neuritis or to a chronic degeneration of the large ganglion-cells or nuclei of the spinal cord (or the nuclei of the cranial nerves). In all three forms certain muscles and muscle groups gradually disappear. The atrophy affects the muscles individually and increases gradually, but an entire extremity does not show diffuse atrophy until an advanced stage of the process has been reached. The muscular power diminishes in proportion to the disappearance of the muscles. This is in contrast with the *atrophic paralyses,* in which the paralysis appears before the atrophy. The question whether a muscular atrophy is myopathic, neuritic, or nuclear is made easier to answer by knowing that each of these forms has a characteristic way of spreading.

(A) Under the *myopathic* form, lately designated by the term *dystrophy,* several groups have been described. Three of the most important are:

1. Erb's juvenile muscular atrophy (progressive muscular dystrophy), which begins in the shoulder-girdle. There are different types of this group.

2. Leyden-Moebius' juvenile form; this begins in the lower extremities. Pseudohypertrophy is closely related to this form. (See p. 999.)

3. Duchenne's infantile variety; this begins in the face.

(B) *Nuclear (spinal) muscular atrophy* begins in the small muscles of the hand and involves early the bulbar nuclei, *i. e.*, produces the picture of bulbar paralysis (better, bulbar atrophy).

(C) The *neuritic* or *neural type of progressive muscular atrophy* is still the least understood. It begins most frequently in the lower extremities, in the domain of the peroneal nerve (peroneal type), and causes a pes varus or equinovarus. Ordinarily, disturbances of sensibility are associated with this form.

Other methods of differentiating these three forms are as follows: *Fibrillary twitching* (p. 956) and *reaction of degeneration* (p. 1023) are demonstrable in the spinal and neuritic forms, but rarely in the myopathic. Disturbance of sensibility, even though very slight, points to the neuritic type. Myopathic muscular atrophy is, as a rule, hereditary, or familial (less characteristic in Erb's type), and affects almost exclusively young individuals. The same is true for some of the neuritic cases; but the spinal form is almost entirely confined to older people without neuropathic heritage.

The examination of the nervous system by means of the newer methods based upon more minute histology of the ganglion-cells will probably determine that the boundaries of the individual forms are in no way so sharply defined as we have thus far assumed. In this regard the entire subject of muscular atrophies, especially neuropathology, needs anatomic revision.

Secondary Degenerative Muscular Atrophies After So-called Atrophic Paralyses.—Paralyses are described as atrophic when the cause of the paralysis deprives the muscles not only of the impulse of the will, but also of the trophic influence of the cells of the nerve nuclei, *i. e.*, the cells of the cord situated in the gray anterior horns.[1]

To avoid confusion with the *simple atrophies of disuse* (p. 999 et seq.), we should remember that the *secondary degenerative atrophies* depend entirely upon a lesion located either in the nucleus or peripherally to it (nuclear and peripheral paralyses).[2] They may be included in the class of paralyses from lesion of the peripheral neuron.

These atrophies ordinarily follow the onset of the paralysis quite rapidly, *i. e.*, within a few weeks. They affect individual muscles very differently, depending upon the degree of the paralysis, and ordinarily attain a very high grade, even to complete disappearance of individual muscles. They present the reaction of degeneration often even before the diminution of volume has become evident. (See p. 1023.) They are also frequently associated with fibrillary twitchings (p. 956). Such atrophies are always an indication of severe paralysis and require a long time for recovery—many months—even in favorable cases. The prognosis is not always absolutely unfavorable in lesions located peripherally to the nuclei, since the regenerative power of peripheral nerves is exceedingly good. The prognosis of the degenerative atrophies which arise from lesions of the nuclei themselves is, on the other hand, absolutely hopeless, because in such cases regeneration does not occur (acute, subacute, and chronic poliomyelitis).

The lack of well-marked appearances of regeneration in these cases, in fact, in any severe focal lesion of the central nervous system, is probably not due to the fact that central nervous tissue possesses less power of regeneration than peripheral. On the contrary, the presence of isolated degenerated fibers in the normal central nervous system, recently demonstrated by Edinger, would indicate that the physiologic wear and tear of the nervous system must be associated with a physiologic regeneration, since otherwise progressive disturbances would result. In fact, even in severe pathologic focal lesions certain anatomic indications of regeneration have been found. That such attempts at regeneration are abortive in severe focal lesions, leading to destruction of tissue, lies in the fact that in them newly formed nerve-fibers find neither a suitable soil nor the proper functional connection to the closely related elements from which they are separated by long distances. If, on the other hand, there be not a severe destructive process, but rather an individual disease of single elements, as, for instance, in the so-called system diseases, the possibility for regeneration in the central nervous system cannot be excluded. Thus the subsidence of paralytic phenomena in acute anterior poliomyelitis is to be attributed to regeneration of those parts in which gross destruction has not taken place; whereas those parts which are involved in the actual inflammatory focus naturally cannot regenerate because of the reasons mentioned above.

[1] The ordinary assumption that these nuclear cells preside over this trophic influence is scarcely correct. However, as centers of spinal reflexes, *i. e.*, of the tendon reflexes, they probably preserve the muscle tonus and prevent a complete muscular inactivity if the muscles are paralyzed above the nuclei.

[2] In reference to the rare cases of degenerative muscular atrophy following lesions of the central motor neuron, and its possible explanation in the extension of the descending degeneration to the peripheral neuron, the reader is referred to the article of Steinert ("Cerebrale Muskelatrophie," Deut. Zeit. f. Nervenheilk., 1903, vol. xxiv, parts 1 and 2).

If a degenerative paralysis does recover, the volume of the muscle gradually returns, following the reappearance of motility and improvement in the electric irritability.

2. TROPHIC DISTURBANCES OF THE SKIN

Ordinary Decubitus.—This occurs in all sorts of severe diseases, and especially in transverse lesions of the spinal cord. It consists of necrotic processes in the skin and subcutaneous tissues of those parts which endure the principal weight of the body while lying in bed—the sacrum, the trocanters, and the heels. In mild cases there is simply an exposure of the corium from destruction of the epidermis; in more severe cases, a deep necrotic destruction of the tissues, even down to the bone. The phenomenon is practically a pressure necrosis. Since decu-

Fig. 385.—Perforating ulcer in tabes. *X*-ray plate showed involvement of the bone (Dr. J. J. Putnam, Massachusetts General Hospital).

bitus is never found in health, we are naturally inclined to consider it due, in a certain sense, to some trophic disturbance, not to an actual affection of trophic centers or trophic nerves, because it is so common in diseases which have no nervous involvement, but rather to the generally depressed nutrition, in which the skin shares. Decubitus is frequent in transverse lesions of the spinal cord, because the enforced quiet is often responsible for impoverished nutrition, the difficulty in moving the patient favors more constant pressure upon the dependent places, and, even if movement be possible, the impaired sensibility prevents recognition of inequalities, such as folds in the bed-clothes, which a healthy person would instantly avoid. Disturbance in the functions of the bladder and rectum, so frequent in these conditions, often keeps the sacral region unclean, and so gives rise to infection. The trophic influence mentioned on p. 1062 (trigeminus), which unques-

tionably passes among the sensory fibers, must also be considered as affecting the sensory conduction of the peripheral neurons.

Acute Unilateral Decubitus.—The trophic influence of the nervous system seems to be more striking in acute unilateral decubitus. This consists of a rapidly increasing necrosis of the skin over the sacrum, which is observed upon the side of motor involvement in severe cerebral hemiplegias, and upon the side of the sensory paralysis in spinal hemiplegias. The unilateral character of the phenomenon shows the influence of the nervous system, but at the same time actual trophic elements of the nervous system are not necessarily responsible. It is quite possible that in cerebral hemiplegias the essential fault is dis-

Fig. 386.—Saber shin (Dr. Joseph Collins, New York City Hospital).

turbance of sensation, which robs the patient of the instinctive protection against considerable pressure upon the anesthetic side. Lesions of the trophic influence of the sensory cutaneous nerves (see p. 1062, trigeminus) must also be considered in sensory disturbances of the peripheral neurons. Acute unilateral decubitus is generally an unfavorable prognostic sign, but merely because it arises only in very marked paralysis; for recovery both as regards life or even usefulness is by no means excluded by the presence of this condition.

Changes in the Skin Over Paralyzed Parts.—The skin over peripherally paralyzed parts, more noticeably the hand, frequently presents a characteristic thin, atrophied, shining appearance—the so-

called *glossy skin.* Conversely, an increase in the subcutaneous fat frequently masks the muscular atrophy, especially in the cerebral, but also in the spinal, paralyses of children.

Other Trophic Changes of the Skin.—It is impossible to discuss here all the changes of the skin which we meet with in diseases of the nervous system. We shall merely mention the presence of pigmentation, of abnormalities in the formation of the epidermis and in the growth of the hair, of deformities of the nails (onychogryphosis), of the loss of the nails (alopecia unguium), of herpes zoster, of symmetric gangrene (maladie de Raynaud, syringomyelia), of panaritium (Morvan's disease; syringomyelia), of Dupuytren's contracture, and of perforating ulcer of the foot. (See Fig. 385.) All these occur predominantly with disease (functional or anatomic) of the peripheral neurons, and for their description we must refer to special pathology.

3. TROPHIC DISTURBANCES OF THE BONES AND JOINTS

In all paralyses occurring in early youth, whether peripheral or central (cerebral and spinal paralyses of children), the growth of the bone

Fig. 387.—Tabetic arthropathy of left ankle (New York City Hospital).

is impeded; on account of such an inhibition of growth and the associated degenerative atrophy of disuse, the paralyzed extremity is much smaller.

An abnormal *fragility* of the bones, which is responsible for the so-called spontaneous fractures, occurs in tabes dorsalis, syringomyelia [and

in elderly individuals who have been confined to bed for a long period of time.—Ed.].

Joint affections are observed in the most diverse diseases of the nervous system. They depend frequently upon purely mechanical causes (stretching a joint by the suspended paralyzed extremity or contractures), yet sometimes they are probably due to actual trophic disturbances. Even here this expression does not mean that the disturbances depend wholly upon a lesion of the nervous system, nor can we consider that a nervous apparatus whose only function is trophic has been affected. (See p. 1062, Trigeminus Peripheral Sensory Fibers.)

Fig. 388.—Tabetic arthropathy of the knee (Dr. Joseph Collins, New York City Hospital).

Perhaps the joint affections which occur in tabes, and which we designate as *tabetic arthropathy*, should be included under such trophic disturbances. (See Figs. 387 and 388.) They are ordinarily characterized by their onset, which is abrupt and painless, by the presence of a considerable fluid, effusion by loosening of the joint, and by a growth of bone and cartilage, leading to deformity of the joint. The knee-joint is most commonly affected, and soon becomes an actual flail-joint. The ankle-joints are also subject to tabetic arthropathy, although not nearly so extensively.

These specific peculiarities of tabetic arthropathies argue against the purely mechanical explanation which has been so frequently assumed, viz., that on account

of the ataxia the joint suffers repeated injuries from which the patient, because of the joint anesthesia, is unable to protect himself. Other reasons for assuming a trophic influence are the characteristic wearing away of the bones (eburnation fracture of the bones in the direct neighborhood of the diseased joint) and their insensibility to tuning-fork vibrations (p. 974). Even here the author does not consider it necessary to assume the existence of special trophic nerves to explain the joint affections and the bone brittleness of tabes, because a sufficient reason for disturbance in growth seems to him to be furnished by the anesthesia of the bones and joint ends, as well as by the occasional involvement of the vasomotor nerves.

J. Wolf's signal work on the "Transformation of Bones" proves incontrovertibly that the structure of the spongiosum is influenced in the most delicate way by the requirements of its work, which, in view of the already proved trophic significance of sensation, can be accomplished so completely either by means of the vasomotor reflexes or because trophic influences pass centrifugally among the sensory fibers through the influence of bony sensibility alone. (See p. 1062, Trigeminus.) It may be considered established beyond question, by physiologic experiments on the variations of the negative current, that sensory fibers also conduct impulses centrifugally and motor fibers conduct centripetally as well.

Acromegaly, a peculiar disease characterized by hypertrophy of the bones of the hands, of the feet, of the nose, and of the lower jaw,

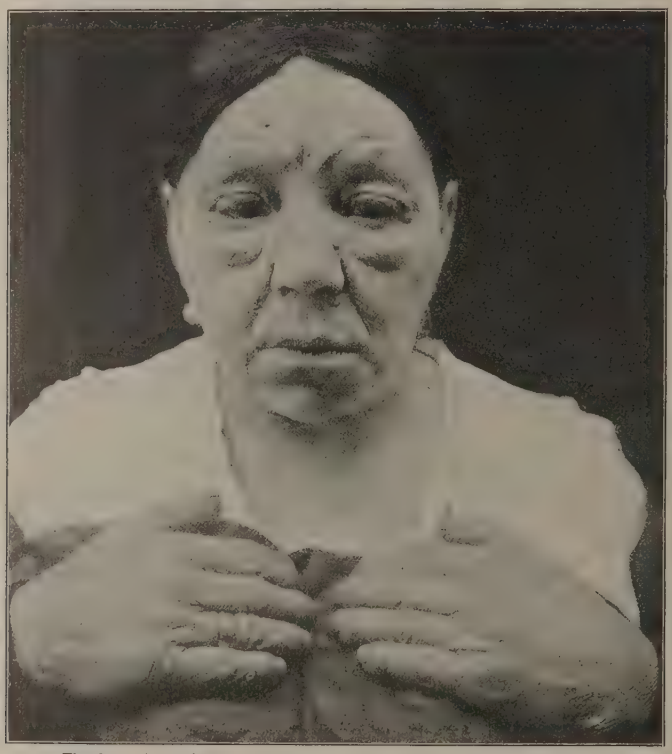


Fig. 389.—Myxedema (Dr. Townsend, Massachusetts General Hospital).

possibly depends upon some trophic disorder of the nervous system. The enlargement is often very marked. The reader is referred to

works upon special pathology for a discussion of its origin and its possible dependence upon an altered internal secretion of the hypophysis cerebri without any other connection with the nervous system.

VI. EXAMINATION OF VASOMOTOR DISTURBANCES

We know so little about the vasomotor relations in nervous disease that it is scarcely worth while to enter upon a general discussion. The author will limit himself to a few remarks, at the same time referring to the section upon the Examination of the Skin (p. 39 et seq.), and to what was said there of local cyanosis.

Vasomotor differences between the paralyzed and the normal half of the body are sometimes found in *cerebral hemiplegias*, especially if the lesion causing the hemiplegia be situated in the pons, peduncles of the brain, or the internal capsule. In the beginning the paralyzed extremities ordinarily appear warmer and redder; later, colder than normal, and cyanotic. What causes these peculiarities is not yet fully understood. Since the cerebrum, as shown by the action of psychic irritation, possesses an influence upon the vasomotors, the initial heat and redness can be explained by assuming a paralysis of the vasomotor tracts of the brain. The vicarious action of the vasomotor centers of the spinal cord, however, quickly changes the condition. The coolness and cyanosis of the skin of the paralyzed side, which appear later and which ordinarily continue as long as the paralysis lasts, probably have nothing to do with the vasomotor action (though this is opposed to the ordinary supposition), but depend upon a stagnation of the venous blood, caused by the immobility of the extremities. Muscular action in movement of an extremity, as is well known, has great influence in propelling the venous blood forward. Perhaps the diminished heat-production in the paralyzed muscles is another factor.

In *transverse lesions* of the spinal cord, the higher the lesion, the more profound is the vasomotor paralysis of the lower half of the body. In lesions of the oblongata, the paralysis of the main vasomotor center and the dilatation of the vessels may lead to a fatal sinking of blood-pressure, accompanied by marked cyanosis and coolness of the peripheral parts. In transverse lesions situated below the oblongata, the paralysis of the vasomotors (vasoconstrictors) affects the territory innervated by that part of the spinal cord situated below the lesion, because the vasoconstrictor impulses of the oblongata, except those supplying the head, run downward through the spinal cord, and leave the cord along with the motor nerves for the same territory, to merge into the sympathetic system. The territory showing motor paralysis then also shows vasomotor paralysis. This is sometimes evident by increased temperature and redness of the paralyzed limb. Yet this paralysis is ordinarily slight and often transitory, because the vasomotor apparatus situated beneath the lesion, as well as the sympathetic fibers of the spinal cord arising above the lesion, are able to functionate vicariously for the nerves which have been cut off. Later, the paralyzed parts frequently become cool and cyanotic on account of the immobility, as in cerebral hemiplegia. *Priapism*, so frequently observed in transverse lesions of the spinal cord, probably depends upon a vasomotor paralysis. The vasoconstrictor fibers of the face probably first issue from the spinal cord in the region of the upper dorsal cord (according to animal experiments on the spinal cord, see p. 1157, Dastre and Morat). Therefore, they may be affected in all lesions of the spinal cord situated above the sixth dorsal nerves. As yet we know nothing definite about the behavior of vasodilator nerves in lesions of the brain and spinal cord.

Tache cérébrale, Trousseau's spots, dermographism, are the different names applied to a cutaneous vasomotor phenomenon which probably depends upon changes in irritability of the vasomotor nerves. It consists of a deep-red color of the skin, often accompanied by the formation of a wheal wherever the skin is irritated, *e. g.*, by light scratching with the finger or the head of a pin. It occurs in purely functional diseases, sometimes in brain diseases (especially meningitis), and not rarely in spinal-cord diseases.

For the description of the peculiar reddening of the skin in *erythromelalgia* and of the mixture of bright red, pallid, or cyanotic discoloration in *Raynaud's disease* we must refer to special pathology.

VII. EXAMINATION OF DISTURBANCES OF SECRETION

Abnormalities of sweat secretion are common, but as yet we cannot accord them much diagnostic significance. Hemihyperhidrosis and hemianhidrosis, *i. e.*, unilateral increase or absence of sweat production, often occur physiologically in otherwise healthy persons. In such a case a suspicion of a disease of the sympathetic system is natural. We also observe hemihyperhidrosis in syringomyelia. In hemiplegias of cerebral origin, sweating of the affected side is sometimes more, sometimes less, marked than upon the healthy side; frequently, however, it is entirely normal. A decided tendency to increased perspiration is often noted in extremities which are affected with an *acute polyneuritis*, even when there is no fever. This is peculiar and of some diagnostic importance.

We know so little about the alteration of urinary secretion in diseases of the nervous system that it is impossible to draw diagnostic conclusions. A pale, abundant urine of low specific gravity (urina spastica) generally follows attacks of *epilepsy* and *hysteria*. *Transitory glycosuria*, or even *diabetes mellitus* ending in death, often accompanies diseases of the brain, particularly when situated in the posterior cerebral fossa. *Diabetes insipidus* has a predilection for neuropathic individuals, especially neurasthenics.

Since anatomists have succeeded in demonstrating nerve-endings in the epithelium of the renal parenchyma, cells which can obviously have a secretory significance only, the relationship of this peculiar disease to the nervous system has become much clearer. (See p. 55.) [An enormous output of urine is sometimes associated with tumors of the hypophysis.—Ed.]

Pathologic variations of the *salivary secretion* are mentioned in the section upon Examination of the Facial Nerve.

VIII. EDEMA IN NERVOUS DISEASES

It is not certain that acute idiopathic edema really depends upon the nervous system, but certainly the name, "angioneurotic" edema (see p. 55), rather prejudices one in favor of such an origin. The edemas which complicate actual nervous diseases are: (*a*) The so-called "*blue edema*" of hysteria. This is discussed under the heading of Angioneurotic Edema (p. 55), and its occurrence was utilized as an argument for assuming that hysteric symptoms are frequently to be attributed to vasomotor disturbances. (*b*) Whether the *edema of the paralyzed members of all kinds of paralysis* is due to vasomotor paresis must be determined in each case; but the immobility and lack of muscular activity leading to venous stasis (as explained upon p. 1007) are generally a sufficient explanation. (*c*) The *edema of the paralyzed members in polyneuritis*. A vasomotor origin in such cases is especially plausible, because if the peripheral vasomotor fibers be involved, the vasomotor disturbance would be exceptionally pronounced, since, as contrasted with cerebral and spinal paralysis, the vicarious action of the auxiliary vasomotor centers, with the exception of those situated on the vessels themselves, is cut off. Still, with the edema of neuritis, we should also consider the possibility of an inflammatory origin.

IX. METHOD OF TESTING THE MECHANICAL IRRITABILITY OF NERVES AND MUSCLES

1. MECHANICAL IRRITABILITY OF MOTOR NERVES

Contraction of a muscle may sometimes be produced by striking the nerve supplying it with a percussion hammer. This occurs in health under the appropriate conditions, *e. g.*, when the nerve runs

superficially upon some firm underlying tissue. This mechanical irritability is increased in *tetany*, especially in the facial nerve (facial phenomenon, Chvostek's phenomenon), and more rarely in *writer's cramp*.

2. MECHANICAL IRRITABILITY OF MUSCLES; IDIOMUSCULAR MECHANICAL IRRITABILITY (Schiff)

Only vigorous percussion will stimulate muscles in health. Such a stimulation causes a sudden, quick contraction of the bundles of fibers which lie in the long axis of the muscles near the point struck. At the same time a smooth local prominence is produced at the spot tapped, or in the long axis of the muscle at a greater or less distance. After a lapse of some seconds this prominence very gradually disappears or first merges into a series of waves running along in the direction of the fibers.

In most *cachectic conditions* (tuberculosis, carcinoma, etc.) the idiomuscular irritability is apt to be increased and the muscular prominence quite pronounced.

The mechanical irritability is also increased wherever muscle exhibits reaction of degeneration with increased galvanic irritability. (See p. 1025.) The longitudinal wave-like contractions are here exceptionally slight, and much slower than the normal. This phenomenon is called mechanical reaction of degeneration.

Curschmann's work[1] should be consulted in regard to idiomuscular mechanical hyperexcitability.

X. METHOD OF TESTING ELECTRIC IRRITABILITY[2]

1. GENERAL DISCUSSION

Electric examination of sensory nerves, including the nerves of special sense, has not yet developed anything of practical value except the method described on p. 976. The following description will therefore be limited to the electric examination of motor nerves and muscles.

For this purpose a faradic (induced, interrupted) or a galvanic (constant) current is employed almost exclusively. One of the many modifications of the Du Bois-Réymond sliding apparatus with one or two zinc-carbon cells will furnish the faradic, while for the constant current the stationary Leclanché batteries are most useful. These latter are expensive and cannot be transported, so that a portable battery with sulphuric-acid-zinc-carbon elements [or one of the standard dry-cell batteries.—Ed.] is better adapted for the practitioner's needs.

Owing to the progress of modern electric technic and the more general use of the electric current, the galvanic batteries for medical purposes have been replaced by apparatus which transforms the ordinary current for medical use. It cannot

[1] Deut. Zeit. f. Nervenheilk., 1905, vol. xxviii, Nos. 5 and 6, p. 361.

[2] Testing the electric resistance of the body, which is essentially dependent upon the condition of the skin, and the standardization of which can be reckoned in milliampères, is no longer of importance in testing electric excitability, because its influence can be reckoned by reading the current strength. (See p. 55, Examination of the Skin.) If the electric findings be reckoned, not by the strength of the current, but by the voltage or by the number of elements, the cutaneous resistance will naturally affect the results. The amount of the resistance can be obtained, according to Ohm's law, by reading the strength of the current, and its influence computed accordingly.

be said, however, that these installations have made electrodiagnosis or electrotherapy more exact. The difficulty lies in the fact that the so-called constant currents obtained from these apparatus cannot always be considered as a single galvanic current, although this is claimed for them. This is true both for the constant current taken directly from the street wire and for the current of a voltage suitable for medical purposes transformed from the alternating current. Many of these so-called constant currents are more or less pulsating, according to the character of the dynamo. The so-called constant currents, which do not flow quite evenly, are not proved, according to the author, equal to the pure galvanic current in a physiologic sense. Many firms utterly disregard this question, and most physicians accept as galvanic the constant currents offered as such without any exact proof of their constancy. It is clear that the existence and number of pulsations in a current can cause essential differences in the effect of the stimulation. The practitioner, however, cannot judge of the more delicate qualifications of such a constant current, and the author considers, speaking generally, that only such central stations are of value for electromedical purposes where the current is taken not directly from the generator, but from large interposed storage batteries. The equalizing effect of interposing the large electric reservoirs of a storage battery will eliminate the physiologic effect of the dynamo pulsation. The author is very skeptical of the results obtained recently with cabinets whenever the current is not in constant connection with a storage battery. To a certain extent the same objections apply to the use of faradic appliances which derive their current from a central station. In this case, however, it has less significance, because the results of faradic tests are only of value for each apparatus at the time of use and absolute standards are in any case excluded.

To maintain, therefore, the reputation for accuracy which electrodiagnosis owes to *the battery current*, it would be highly advisable to use the current known, technically, as a constant current, to store local storage batteries whenever the central station is not so supplied, in place of the older cell batteries. To the convenience of a stationary storage battery as against the ordinary galvanic battery should be added the absolute certainty of having an actual galvanic current, *i. e.*, a perfectly constant and non-pulsating current.

The diagnostic application of the so-called sinusoidal current has been studied too little from a scientific standpoint to be discussed here.

For stimulation we employ flat electrodes or those terminating in a bulb. They are covered with chamois leather, and before being used should be moistened with warm water. If salt be added to the water, the current strength is increased, but the electrodes soon become tarnished and spoiled. Different sizes of button-shape and flat electrodes are required, and some of the former should be made with a contact contrivance for opening and closing the current.

For an accurate electric examination we need an appliance to measure the strength of the galvanic current. Until recently this purpose has been served by a galvanometer divided, according to the absolute strength of current, into milliampères. The apparatus of Gaiffe (Paris), Edelman (Munich) [or Edison (New York).—Ed.] can be recommended. The galvanometer is an essential for electrotherapeutic purposes; but the voltmeter offers many advantages for electrodiagnosis. (See later, p. 1015 et seq.)

Medical batteries are supplied with a commutator, or current changer, for quickly changing the poles, and with a contrivance for connecting or disconnecting the individual cells in order to increase or decrease quickly the strength of the current. Finer gradations are obtained by inserting a fluid rheostat into the main circuit. Although quite practical with the ordinary galvanometer, a rheostat in the main circuit cannot be used with the voltmeter, *i. e.*, a galvanometer with a very strong resistance in the lateral circuit, and so is not practicable for diagnostic purposes. If we use the voltmeter, we must employ either a rheostat in lateral circuit or, still better, the "Gaiffe reducteur

de potentiel." If the street current be used, the reduction occurs also by means of the potential reducer or the volt regulator.

The faradic current is reduced by approximating the secondary coil to the primary. Faradic stimulation means stimulation with a free swinging interrupter; that is, with a rapidly alternating current (tetanizing stimulation). The apparatus can also be used to produce single induction shocks, by fastening the Neef hammer and opening and closing the primary current manually. This is of very great practical advantage because, in peripheral palsies, especially those with greatly diminished excitability, this method produces much less pain than the tetanizing form. Besides, degenerating muscles react longer to single interruptions than to the tetanizing alternations, a very important therapeutic point in the treatment of paralyses.

The polar method of electric stimulation is nowadays ordinarily employed for electric examination. One pole is placed upon the spot to be stimulated, the other upon an indifferent spot, as far distant as possible, *e. g.*, upon the abdomen or the breast. The examination is thus essentially simplified by disregarding the direction of the stream. For all practical purposes both poles of the faradic current may be said to act alike, although not with equal strength. With the galvanic current, on the other hand, there is a fundamental difference between the two poles. This difference is apparent in the so-called laws of contraction of motor nerves and muscles. The cathode of the opening induction current acts most powerfully; therefore it is agreed to employ this for faradic stimulation. On the other hand, in every case where we use the galvanic stream, we must test cathode and anode stimulation separately and compare the results.

The active electrode should not be too large if the object be to stimulate isolated nerves or muscles. Too small electrodes are impracticable, because with them the intensity of the current is so great that the pain of the examination is materially increased. For most purposes a button-shaped electrode of 1 to 2 cm. diameter answers the purpose. If we wish to compare the results of different electrodiagnostic examinations, uniform electrodes should be used, since the stimulation effect depends not only upon the strength, but also upon the intensity of the current. (See p. 1019.) Erb and Stintzing recommend so-called normal electrodes for all electric examinations. Erb's normal electrode is 10 sq. cm. in size (a circular surface of 3.6 cm. diameter). Stintzing's electrode, which is serviceable for stimulating small muscles (*e. g.*, of the hand), has a circular surface of 3 sq. cm. (1.8–2 cm. diameter). The indifferent electrode should be as large as possible, in order to decrease the intensity of the current through it, even when a strong current is employed, and so to lessen the pain caused by the passage of the current. The pain is due essentially to electrolizing the skin.

There are some exceptions to the rule given above, that the indifferent, large electrode should be applied as far as possible from the point to be stimulated. These exceptions occur frequently enough to merit mention, *e. g.*, when employing strong currents in diminished irritability, if we should apply the indifferent electrode to the abdomen and then attempt to stimulate the small muscles of the hand, the effect would be very confusing. The current passing through the nerves and muscles of the arm would produce contraction of the muscles not only of the hand, but also of the arm; the entire arm would naturally be jerked

about, and so confuse us. In such a case it would be better to apply the indifferent electrode to the other surface of the same hand. The employment of the largest possible indifferent electrode establishes a great difference in current intensity between the two electrodes, so that an almost exclusive, and practically a polar, action results at the differentiating electrode. Such devices should be made use of upon other parts of the body.

A complete electric examination, evidently, must include testing each muscle and nerve. It consumes a great deal of time, because control tests must be made in order to verify results. In fact, the electric examination of an extensive paralysis requires more time, skill, and patience than any other kind of examination, if it be accurate and thorough, and leads to many serious errors if it be carried out hastily or carelessly. An accurate testing of one muscle is of more service than the careless examination of all the paralyzed muscles. Multum is better than multa; quality, than quantity. A complete examination of all the muscles implicated in a paralysis is impracticable for a busy practitioner, especially if, in the interest of prognosis, continued changes in the reaction during the course of the disease are to be followed. Testing some few muscles and nerves is, fortunately, sufficient for diagnostic purposes.

A complete electric examination of a nerve muscle should include testing of both muscle and nerve by the galvanic as well as by the faradic current. A nerve generally reacts the same to galvanism as to faradism, so that, if anything has to be slighted, it is advisable to omit the galvanic test. Still, the latter has here, as elsewhere, a distinct advantage over faradism, because with it the amount of stimulation can be measured.

There are certain places scattered over the surface of the body which, when stimulated by a small electrode, evoke the best response from one definite nerve or muscle. These are the so-called "motor points" determined by Duchenne, Erb, von Ziemssen, and others, and make possible the individual stimulation of single motor nerves and muscles. They are represented in the accompanying figures (Figs. 390 to 394). Their location has been confirmed by the author's own examinations. Most motor points for nerves are situated where the nerve lies superficially and at some distance from other nerves. The motor point of a muscle is usually at the point where the motor branch of the nerve enters the muscle belly. In point of fact, the nerve is here stimulated also; therefore, when endeavoring to obtain a pure muscular reaction, it is a good plan to keep as far as possible from the motor points, unless the nerve irritability be lost. In this way stimulation will produce local contractions only in the individual bundles which are stimulated.

In all electric tests it is essential to determine three factors: First, whether both the motor nerve and the muscle still react to the faradic and to the galvanic current; secondly, whether the reaction to either current be quantitatively altered, *i. e.*, whether it be increased or, as most frequently happens, diminished; and, finally, whether any qualitative alteration in irritability can be demonstrated, *i. e.*, any deviation from the ordinary type of contraction. With the galvanic current the effect of each pole must be noted.

The "dosage," *i. e.*, the strength of current employed, must always be estimated in examining for quantitative changes.

This has been done heretofore in using the galvanic current by reading the strength of the current. The latter may change so very rapidly

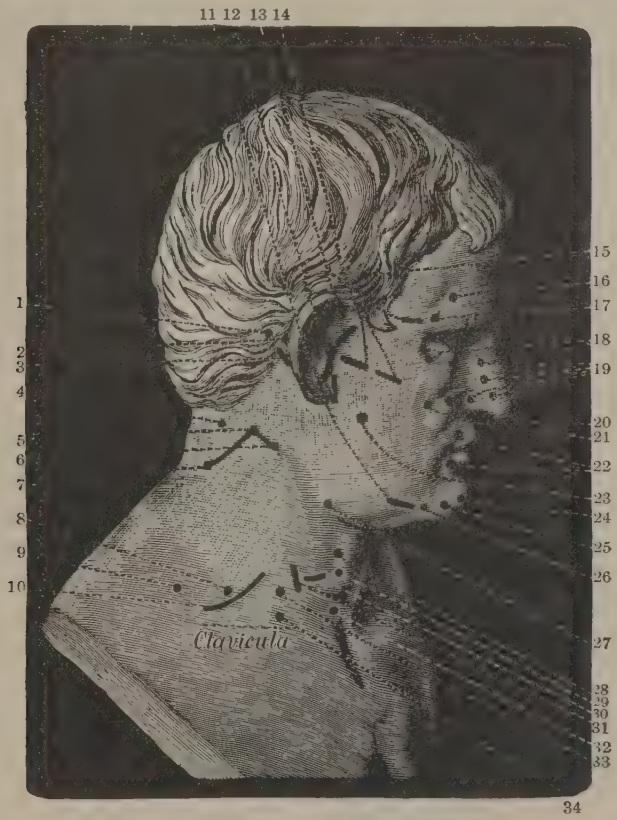


Fig. 390.—Motor points on the head and neck.

1. Occipitalis.
2. Retrahens aurem.
3. Posterior auricular nerve.
4. Splenius.
5. Spinal accessory nerve.
6. Sternocleidomastoid.
7. Trapezius.
8. Circumflex nerve (deltoid).
9. Long thoracic nerve (serratus magnus).
10. Brachial plexus.
11. Lower branch.
12. Facial nerve (trunk).
13. Upper branch.
14. Middle branch.
15. Temporalis.
16. Frontalis.
17. Corrugator supercilii.
18. Orbicularis palpebrarum.
19. Nasal muscles.
20. Levator labii superioris.
21. Zygomaticus major.
22. Orbicularis oris.
23. Masseter.
24. Levator labii inferioris.
25. Depressor labii inferioris.
26. Depressor anguli oris.
27. Hypoglossal nerve (in the depths).
28. Platysma.
29. Sternohyoid.
30. Omohyoid.
31. Phrenic nerve.
32. Sternothyroid.
33. Erb's point[1] (deltoid, biceps, brachialis anticus, supinator longus).
34. Anterior thoracic nerve (pectoralis major).

that in closure contraction it must be read immediately. In examination of the opening contraction, it is read just before the contraction

[1] Erb's point is situated 2 to 3 cm. above the clavicle, somewhat to the outer side of the posterior border of the sternocleidomastoid, immediately in front of the transverse process of the sixth cervical vertebra.

begins. Before taking the reading, the current should be allowed to flow through the body and the galvanometer until the needle of the

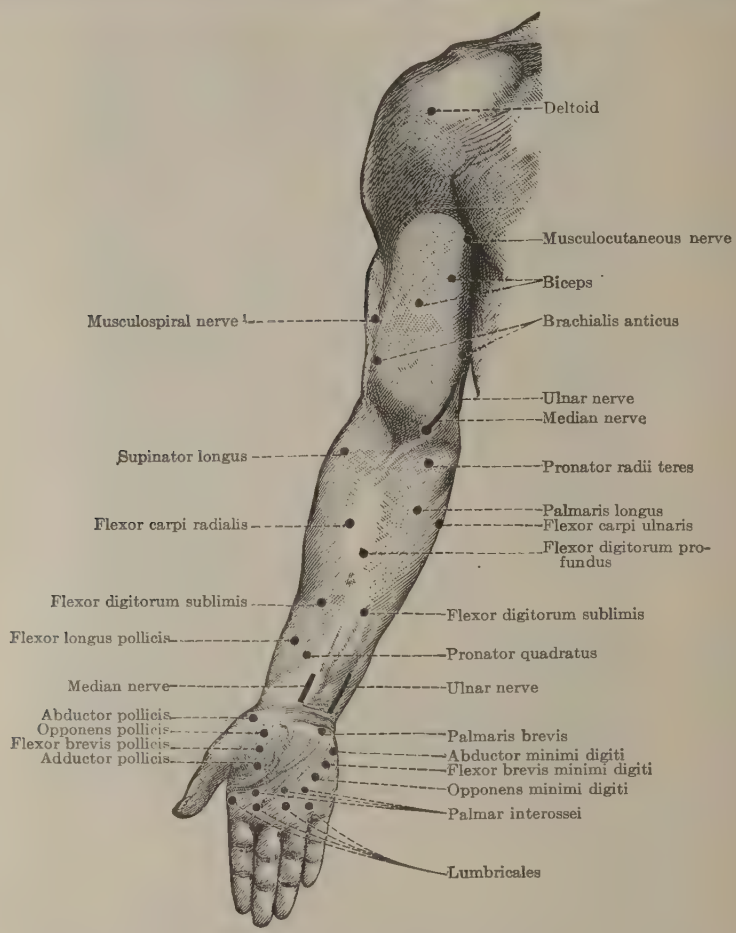


Fig. 391.—Motor points on the anterior aspect of the arm.

latter becomes quiet. In a well-made instrument adapted for medical purposes, with a good rheostat, this will occur in a few seconds.

[1] This point should be sought for in the external bicipital groove at the junction of the middle and lower thirds of the arm. According to Erb, it is midway between the external condyle and the insertion of the deltoid. It is frequently difficult to locate, because the nerve easily rolls from beneath the electrode, and possibly also because the electrode is lifted away from the nerve by the contraction of the biceps and triceps. A very small electrode should be employed for this examination. It should be noted that the trunk of the musculospiral nerve may also be irritated in the axilla at the inner border of the upper extremity of the coracobrachialis. Erb's point (see Fig. 390) may also be employed for the supinator longus. These points possess a special clinical interest, as will be shown on p. 1031.

Dubois (Bern) [1] has recently shown, however, that in estimating the galvanic irritability of a nerve or muscle it is more accurate to make the calculation in volts than in ampères, for the same movement of the muscles always takes substantially the same voltage, while the current rises with the resistance interposed. This coincides with the experience

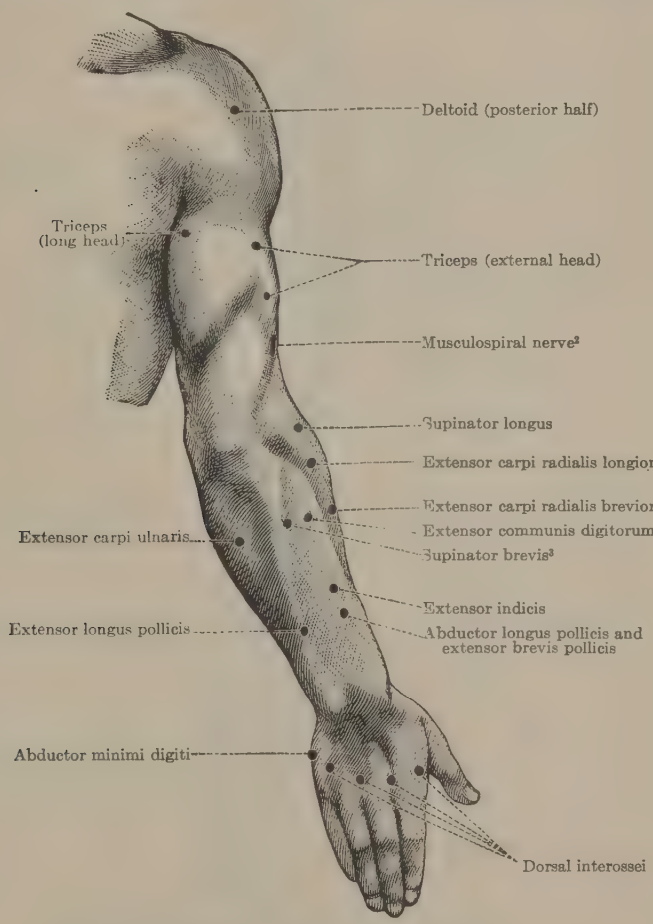


Fig. 392.—Motor points on the posterior aspect of the arm.

of Cornaz,[4] one of his pupils. He found that the measurements made in volts conformed much more nearly than those made in ampères when he tested the same nerve of the same individual at different times,

[1] Arch. de physiol., October, 1897. [2] See note to Fig. 391.

[3] It is possible to irritate the supinator brevis by itself only when the extensor communis digitorum is atrophic and fails to respond to the electric current (as in lead palsy, for example). [4] I. A. Diss., Bern, 1898.

or similar nerves of different people, or similar nerves of the two sides of the body. Dubois explains this phenomenon by the following fact, which he established experimentally (for the details his monograph must be consulted): The resistance of the human body, in consequence of its great "capacity," has practically no influence on the amount of stimulation, which depends upon potential. So that if the metallic resistance

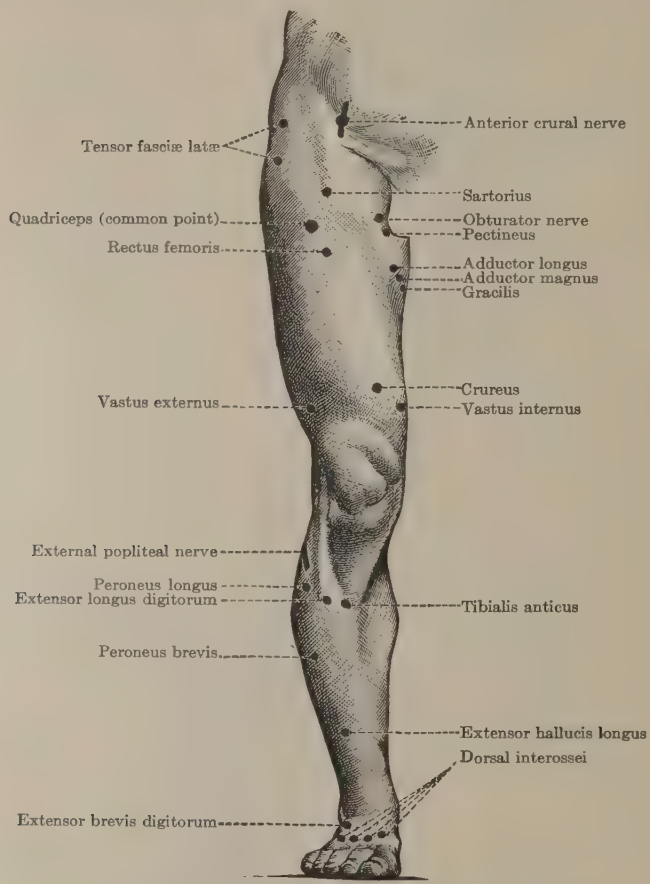


Fig. 393.—Motor points on the anterior aspect of the leg.

of the current circuit do not change, and if the current strength vary only with alterations in the electromotive force, the stimulation can be determined with considerable accuracy by the volt tension. To be sure, this is no longer the case if rheostat resistance be interpolated into the main circuit and the action of the current is thus graded, as was formerly the custom in electrodiagnosis. Dubois has shown that such resistance, whether fluid or metallic, produces strong auto-induc-

tion. Therefore it must cause a change not only in the current strength, but also in the increase of the current. Under these conditions neither the volt tension nor the current strength can be considered a measure of the irritative effect, so that this old procedure loses its value. Examining the same muscle repeatedly with the same strength of current,

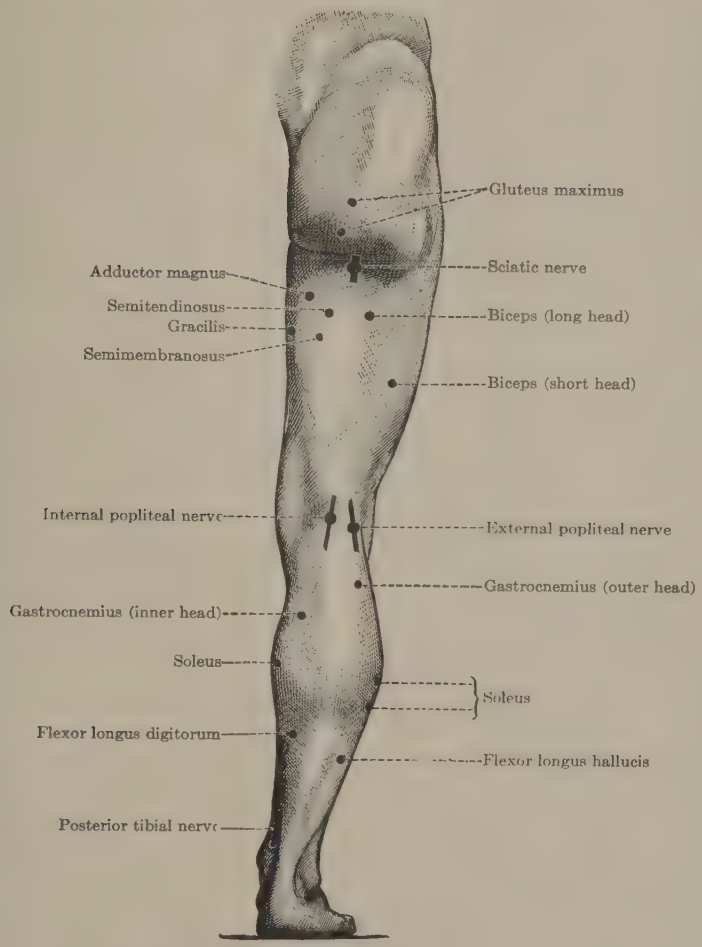


Fig. 394.—Motor points on the posterior aspect of the leg.

but with varying rheostat resistance, would therefore explain many previously inexplicable contradictions in electrodiagnosis.

Hence, in employing the voltmeter it is advisable to regulate the galvanic apparatus so that the resistance in the main current will not vary with a gradation of current activity. In other words, in addition to the employment of the element transformer, the current activity

should be graded only by altering the volt tension. The latter effect can be accomplished by inserting a rheostat into the lateral circuit, or, still better, by Gaiffe's "reducteur de potentiel," constructed according to the principle of the rheochord.

Instead of the galvanometer, Dubois recommends substituting the voltmeter, combined with the "reducteur de potentiel," for electrodiagnosis (though not for electrotherapy). The voltmeter is practically a galvanometer situated in the lateral circuit, but of so great a resistance that the resistance of the battery does not enter into consideration. Gaiffe's instrument is especially serviceable for electrodiagnostic purposes, because a simple alteration will in a few seconds change it to a galvanometer with *accurate divisions*. The voltmeter possesses another great advantage. Its needle does not oscillate with the opening and closing of the current, so that the reading may be made during the examination. This is much more trustworthy than the estimation of the current strength, which can be read only after the stimulation is finished or with the opening stimulation before it begins.

This combination of voltmeter with "reducteur de potentiel" has been used at the author's clinic as long as batteries[1] have been employed, and has been entirely satisfactory.

It should be noted that the accuracy of the measurement of galvanic reaction by means of the voltmeter has recently been questioned by Mann,[2] who recommends, as the method most free from objection, the employment of condenser discharges. Since this method has not yet been extensively employed, the author will simply refer the reader to Mann's article, and also a later monograph by Zanietowski, The Condensor Method, Leipzig, Barth, 1906.

The condensor method causes much less pain than the galvanic test on account of the short duration of the current and the absence of electrolytic effects. It would be an especially desirable substitute in those cases of peripheral paralysis where, because of greatly lowered excitability, very strong galvanic currents are necessary. The investigations undertaken by the author in the interest of electrotherapy rather than diagnosis have shown that the condenser stimulations act incompletely if the excitability be *low*, *i. e.*, fail to excite contractions that might still be produced by the galvanic current. Dubois has shown that if the excitability be normal, a condenser of one microfarad with about the same voltage causes a contraction similar to that of the galvanic current.

The induction current, as Dubois has shown, has faults, even with the modern simplified gradations of the apparatus. Unfortunately, it must be confessed that thus far no method has been devised to estimate the physiologic action of the induction current in a universally efficient way, *i. e.*, in figures independent of the apparatus employed. The physiologic action of one induction apparatus cannot be compared with the action of another, so that for quantitative examination or for comparison of results we should always employ the same apparatus and the same primary voltage. In case cells are used for the induction apparatus it is necessary to have always the same number (2 or 3) of Leclanché or Bunsen elements. If the induction apparatus be connected with the street current, the amount must be set at a definite voltage. The distance that the secondary coil is moved will measure the current strength; provided, of course, that the elements or cells are freshly prepared. Since the individual centimeters of the scale usually placed upon the induction apparatus correspond to entirely different

[1] At the present time a Klingelfust apparatus connected with central storage batteries is used.

[2] Berlin. klin. Woch., 1904, No. 33.

variations in the effect of the current, it would be much better to graduate the scale also in absolute units, according to the method of Kronecker.[1] It must not be supposed, however, that such a graduation will enable us to compare different induction apparatuses, since the rapidity of increase in the individual induction currents, and their consequent irritating effects, are quite different, being dependent upon the quality of the coils as well as upon the electromotive force of the elements which run the apparatus. The absolute graduation simply possesses the advantage that, if we always use the same machine with freshly prepared elements, we obtain a better idea of the effect of the current.

Even with a faradic current the bodily resistance varies physiologically, because the stimulation takes place under variable conditions in a circuit of great capacity; but such variation does not produce any decided difference in the effect of the stimulation any more than with galvanism (see above). Therefore it seems unnecessary to follow the advice of some writers and measure the skin resistance galvanically, as well as the distance of the secondary coil, when applying the faradic current. But in any event the electrodes must be well moistened, in order that the contact may be as complete as possible.

It is quite as important, in determining the dosage of the faradic as in determining that of the galvanic currents, to employ electrodes of definite size; because, naturally, the intensity with which the current impinges upon a given spot is quite as important as the current strength and the voltage. The current intensity is equal to the current strength divided by the square surface of the electrode. Therefore, under otherwise equal conditions, an electrode of 2 sq. cm. surface provides only half as great a stimulation effect as one of 1 sq. cm. surface. Such an estimation is accurate only for the skin surface directly in contact with the electrode. In penetrating the skin the current is, of course, diffused over a much greater area, and since most of the muscles and nerves to be stimulated lie at a certain depth, the size of the electrode is in reality not so important as implied by this calculation. At all events, in order that the conditions may be kept as constant as possible, electrodes of the same size should be employed in comparative examination, and their dimensions should be mentioned in the description. The so-called "normal" electrodes (p. 1011) are the most satisfactory.

The technic of applying the electrode is naturally important, for a larger electrode set against the body surface at an angle naturally acts like a smaller one. Again, one-sided pressure should be avoided, the pressure should not crowd the soft parts too much, and the well-moistened surface of the electrode should be in intimate contact with the body.

If, as is sometimes the case, especially in employing a portable galvanic battery, we wish to differentiate the poles quickly, it can be done very easily by grasping the electrodes, one in each hand, and then estimating which electrode causes more intense burning on closing the current. The one that does will be the cathode. Of course, the electrodes should be of the same size and equally well moistened. Again, the cathode turns moistened violet litmus-paper blue; the anode turns it red. With the faradic current a stronger irritation is produced by a cathodal opening, and after the passage of some current a blue spot will appear upon the litmus paper. The opening of the induced current, on

[1] Zeits. f. Instrumentenkunde, 1889.

account of its greater strength, is of chief importance for the collective action of the alternating stream.

The electrode to be employed in such tests should be of polished metal; for this will give sufficient current strength for the slight electrolytic action of the induction current; and we need not fear any discoloration of the litmus paper by the acid metallic salts which always collect upon old electrodes.

The following abbreviations are employed to tabulate the results of an electric examination:

X mm. *D* = distance in millimeters that the secondary has been withdrawn from the primary coil.
M.A. = milliampères.
V. = volt.
Ca.C.C. = Cathodal closure contraction.
An.C.C. = Anodal closure contraction.
An.O.C. = Anodal opening contraction.
Ca.O.C. = Cathodal opening contraction.
Ca.C.T. = Cathodal closure tetanus.
Ca.C.C. = 2 *M.A.* signifies that a minimal cathodal closure contraction will be produced by 2 milliampères of current.
Far. C. 90 mm. *D.* signifies that a minimal faradic contraction will be excited when the secondary coil is withdrawn 90 millimeters.
Ca.C.C. > *An.C.C.* signifies that the cathodal closure contraction is greater than the anodal closure contraction, etc.

2. METHOD OF TESTING THE QUANTITATIVE ELECTRIC IRRITABILITY OF THE NERVE MUSCLE

We test the quantitative electric irritability of a nerve or of a muscle by estimating how strong a galvanic, and then how strong a faradic, current is required to produce a minimal contraction. (See p. 102 et seq.) With a galvanic current the cathodal closure contraction is normally the easier to obtain; hence, it is ordinarily employed for this estimation. When a maximum current produces no further contraction, the condition is called exhausted irritability. Since this condition holds good only for that particular maximum current strength or volt tension employed, it is advisable to determine and note both of them.

Physiologically, the irritability of different nerves and muscles, as well as that of the same muscle or nerve, varies considerably in different individuals. It is not by any means easy, therefore, in any given case to determine whether the results of the examination overstep the normal limits, and, if so, how much. The following method seems the most practical: We estimate the irritability and then compare it with that of a healthy person, or, if the disturbance be unilateral, with that of the healthy side. The latter is, of course, always more accurate. Symmetric points and an identical position must, of course, be selected. Erb and Stintzing have shown that the normal differences in irritability upon the two sides are very slight. In comparing the results with those found in a healthy person, decided differences only should be regarded as significant.

Galvanic Current

Normal Estimations to be Used in Comparing the Galvanic Irritability of the Two Sides.—The following figures represent the maximal differences of the galvanic current strength which is needed to stimulate actively the normal nerve of both sides of the body. They are copied from Stintzing, and were estimated with his normal electrode of 3 sq. cm.:

Maximal Physiologic Differences between the Galvanic Irritability of the Two Halves of the Body Expressed in Current Strength. (After Stintzing.)

Ramus frontalis of the facial nerve	0.7	M.A.
Nervus accessorius	0.15	"
Nervus medianus	0.6	"
Nervus ulnaris (2″ above the olecranon)	0.6	"
Musculospiral nerve	1.1	"
Nervus peroneus	0.5	"
Nervus tibialis	1.1	"

The following figures show that the voltage rates, according to Dubois and Cornaz, are more conclusive. These writers found, after many examinations:

Rates of Voltage Which are Required for a Minimal Stimulation of the Corrosponding Normal Nerves of the Two Sides of Body.

Facialis (maxim.)	100 : 122	(corresponding ratio of current strength	= 100 : 129)
Medianus "	100 : 117	(" "	= 100 : 503)
Musculospiral "	100 : 112	(" "	= 100 : 145)
Ulnaris "	100 : 116	(" "	= 100 : 253)
Peroneus "	100 : 130	(" "	= 100 : 175)

Normal Estimations to be Used in Comparing the Galvanic Excitability of Different Individuals.—The following figures represent the averages which Stintzing computed from an examination of 58 healthy individuals. They are useful when we cannot compare the two sides of the body:

Limits of the Normal Irritability Expressed in Current Strength. (After Stintzing.)

Ramus frontalis of the facial nerve,	irritated by	0.9 — 2.0	M.A.
Ramus zygomaticus of the facial nerve,	"	0.8 — 2.0	"
Ramus mentalis,	"	0.5 — 1.4	"
Nervus accessorius,	"	0.1 — 0.4	"
Nervus ulnaris 2″ above the olecranon,	"	0.2 — 0.9	"
Musculospiral nerve,	"	0.9 — 2.7	"
Nervus peroneus,	"	0.2 — 2.0	"
Nervus tibialis,	"	0.4 — 2.5	"

Here also the following figures show that the results of the rate of voltage according to Dubois and Cornaz are more reliable.

Limits of the Physiologic Irritability of Corresponding Nerves of Different Individuals and of the Same Individual at Different Times, Expressed in Voltage and in Current Strength.

MAXIMAL DIFFERENCES.

	Volts.	Ratio.	Milliampères.	Ratio.
Facialis.				
1. In different individuals,	3.8 — 9.4	(100: 274)	0.8 — 3.0	(100: 375).
2. In the same individual at different times,		100: 126		100: 190
Medianus.				
1. In different individuals,	4.4 —14.2	(100: 323)	0.2 — 2.7	(100: 1350).
2. In the same individual at different times,		100: 212		100: 1000
Musculospiral Nerve.				
1. In different individuals,	5.2 — 12.8	(100: 246)	0.8 — 2.5	(100: 246).
2. In the same individual at different times,		100: 152		100: 225
Ulnaris.				
1. In different individuals,	1.6 — 7.8	(100: 487)	0.1 — 1.9	(100: 1900).
2. In the same individual at different times,		100: 260		100: 575
Peroneus.				
1. In different individuals,	4.0 — 10.5	(100: 265)	0.6 — 1.8	(100: 300).
2. In the same individual at different times,		100: 225		100: 225

When a weaker current strength or voltage excites a minimal contraction, the excitability is increased; when a stronger one is required, the excitability is diminished.

As mentioned above (see p. 1015), the measurement by voltage is the more accurate method, *e. g.*, a minimal voltage which will produce the necessary stimulation will correspond to a much greater current strength if the resistance be slight than if the resistance be high (according to p. 1016 et seq.). The milliampère value will, in the former case, conceal a diminished, and, in the latter case, an increased, excitability.

Faradic Current

Every examiner will gradually become accustomed to his own apparatus, so that he knows what differences come within physiologic limits. Stintzing found that with his own apparatus the maximal physiologic difference for all nerves examined was 15 mm. D. This is a rather indefinite statement, since this 15 mm., even with Stintzing's apparatus, corresponds to entirely different amounts of irritation, dependent upon the position of the secondary coil, and these values, moreover, do not obtain when another apparatus is employed. Differences which exceed a physiologic maximum should be regarded as pathologic. If a shorter distance be necessary to excite a minimal contraction, it shows a diminution of irritability; if a greater distance be required, an increase of irritability.

3. METHOD OF TESTING THE QUALITATIVE ELECTRIC EXCITABILITY OF THE NERVE MUSCLE

The irritability of motor nerves is subject only to quantitative alteration. But with the muscles, quantitative changes are often accompanied by qualitative alterations, which require a special description.

(*a*) Normal Conditions

The qualitative normal reaction of motor nerves and muscles to a galvanic stimulation is expressed in the following so-called law of contraction:

The Normal Law of Contraction for the Motor Nerves with a Galvanic Current.

WEAK CURRENT

Ca.C.C. ..... *An.C.* : no effect.
Ca.O. : no effect ..... *An.O.* : no effect.

MODERATE CURRENT

Ca.C.C. : vigorous ..... *An.C.C.* : weak.
Ca.O. : no effect ..... *An.O.C.* : weak.

VERY STRONG CURRENT

Ca.C.T. ..... *An.C.C.*: vigorous.
Ca.O.C.: variable ..... *An.O.C.*: vigorous.

The normal law of contraction for the muscles with a galvanic current differs from the above only by the fact that the opening contraction is either obtained with great difficulty or, more commonly, cannot be produced. The contraction of a muscle to galvanism, whether the muscle be stimulated directly or indirectly through the nerve, normally appears

very suddenly. Yet some differences occur, depending upon whether the differential electrode be applied to the motor point of the muscle or at some distance from it. The latter (avoiding the motor point as far as possible) is the only way in which we can excite a pure muscular contraction. Although sudden, the contractions are somewhat less lightning-like, and the distinction between *Ca.C.C.* and *An.C.C.* is less pronounced. A stimulation from the motor point itself should be regarded as the stimulation of a nerve. In case the nerve excitability is not lost, we must consider stimulation of a motor point in reality a nerve stimulation. In spite of this, the excitability of a motor point is usually designated in electrodiagnosis as muscular excitability.

Normal Laws for Contraction of Motor Nerves and Muscles with the Ordinary Faradic Current (the Rapidly Interrupted and Alternating Induced Current).—Faradic stimulation of both muscle and nerve is tetanic, *i. e.*, as soon as *D.* (the distance) is diminished enough to produce any contraction at all, the muscle remains contracted so long as the alternating current flows through it or through its motor nerve. The onset and the cessation of the tetanic muscular contraction correspond to the closure and the opening of the current, and are sudden and lightning-like. The two poles of the faradic current differ only in their quantitative effect, *i. e.*, the pole at which the opening induction current has its cathode is somewhat stronger. The faradic current, when applied at some distance from a motor point, produces a much weaker contraction than when applied directly to it. Qualitatively, on the contrary, the effect is identical.

(*b*) Pathologic Conditions

Reaction of Degeneration (R. D.).—The essential factor in the reaction of degeneration which occurs in peripheral and nuclear paral-

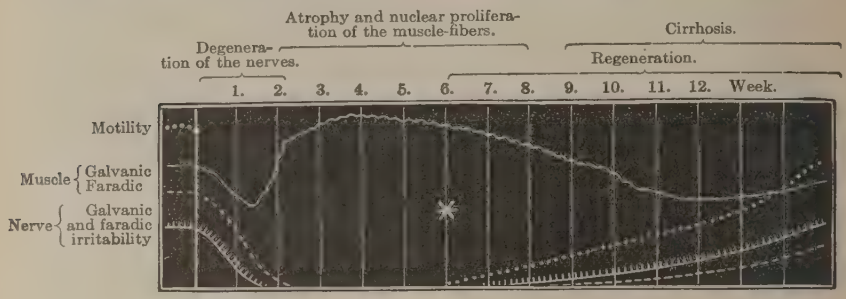
(*a*) Healthy girl. *Ca.C.C.* decidedly greater than *An.C.C.* Contraction lightning-like.

(*b*) Poliomyelitis reaction of degeneration. *An.C.C.* much greater than *Ca.C.C.* Contraction slow.

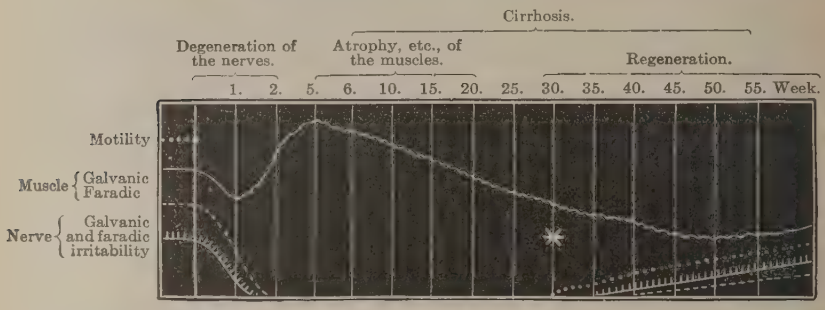
Fig. 395.—Myographic curves of galvanic closure contraction from a direct muscular stimulation in the peroneal region: (*a*) Normal; (*b*) reaction of degeneration (taken from Kast).

yses is the condition of the muscles (see p. 1029 et seq. in regard to its significance). This reaction, in the broadest sense of the term, presents very different modifications. The two cardinal symptoms common to all forms are the following:

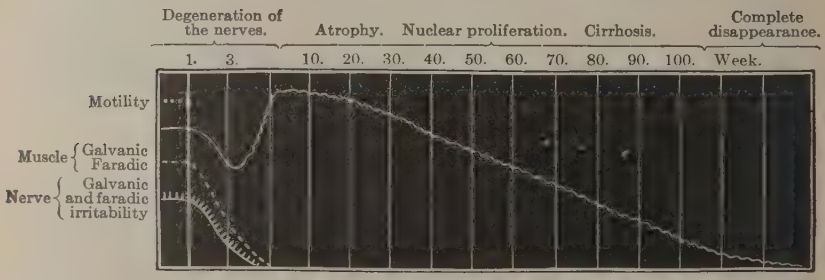
1. The essentially different reaction of the muscle to prolonged and to transitory stimulation, that is, to galvanic and faradic. The muscle



(*a*) Paralysis with a relatively early recovery of the motility.



(*b*) Paralysis with a later recovery of the motility.



(*c*) Irreparable paralysis. Disappearance of motility persists.

Fig. 396.—Diagram of the course of irritability in peripheral paralysis with complete reaction of degeneration: The wavy character of the line which represents the galvanic irritability signifies that the irritability is qualitatively modified, *i. e.*, there is a R. D. Where the line is even, the condition is qualitatively normal. The asterisk marks the return of voluntary motility. The histologic changes in the nerve and muscle are printed at each stage above the curves. The figures above the curves correspond to the number of weeks which have elapsed since the onset of the paralysis. The abscissæ of the later course of the paralysis had to be shortened in different degrees for the three curves on account of the space, so that the curves cannot be exactly compared as to their length (Erb).

either does not react at all to the faradic current, or its reaction is very much weaker than to the galvanic current. Dubois's experiments, how-

ever, show that single shocks of a very strong current will often produce a contraction, even where the reaction of degeneration is complete. He believes that rapidly succeeding shocks, *i. e.*, with a freely vibrating hammer, so fatigue the muscle that it cannot contract.

2. The contraction no longer exhibits a lightning-like character, but is slow and vermiform. An after-contraction may sometimes persist after the original effect has ceased; and in a pronounced example a tetanic contraction will be excited which will persist most of the time while the current is applied.

The other characteristics of the reaction are very variable; they will be mentioned below.

The two peculiarities just outlined are common to all forms of reaction of degeneration, and are to be regarded as the clinical expression of a degenerative atrophy of the muscle due to some peripheral lesion. (See p. 1029 et seq.)

The complete reaction of degeneration may be schematically described as follows:

Faradic test: Excitability of the nerves lost.

Faradic test: Excitability of the muscles lost.

Galvanic test: Excitability of the nerves lost.

Galvanic test: Excitability of the muscles immediately after the onset of the paralysis quantitatively normal, later increased, and finally often decidedly diminished. The contraction is slow. Myobradia, *An.C.C.* is excited more rapidly than *Ca.C.C.* *An.C.C.* > *Ca.C.C.* for the same current strength or voltage.

The myographic curves (Fig. 395) illustrate these quantitative changes of the muscle reaction.

The duration of complete reaction of degeneration in peripheral paralysis is very typical. It has been studied thoroughly in severe facial paralysis of rheumatic origin, and has been graphically represented by Erb (Fig. 396).

Mechanical reaction of degeneration, mentioned upon p. 1009, occurs principally where there is complete electric reaction of degeneration with increased irritability.

Partial (Incomplete) Reaction of Degeneration.—In this form the faradic and galvanic irritability of the nerves and the faradic irritability of the muscles are not lost, but merely diminished. A slow contraction is ordinarily caused only by galvanic excitation of the muscles, although sometimes faradic excitation with isolated shocks at some distance from the motor point will produce the same effect. A scheme of the incomplete reaction of degeneration follows:

Faradic: Nerve, Muscle. *Galvanic:* Nerve.	Irritability merely diminished. Contractions not slower except sometimes in the case of the faradic muscle contraction when the motor point is avoided.
Muscle.	Far from motor point like the complete reaction of degeneration.

The course of an incomplete reaction of degeneration in peripheral paralyses is represented in Fig. 397.

Incomplete Reaction of Degeneration with Compulsory Indirect Sluggish Contractions.—In this form, as distinguished from the simple incomplete reaction of degeneration, all the contractions are slowed, not only those excited by galvanic muscular stimulation, but also those excited by faradic stimulation of the muscles and by faradic or galvanic stimulation of the nerves.

Mixed Reaction of Degeneration.—When some of the fibers of a muscle preserve a normal reaction, while others present a reaction of degeneration, the result is called a *mixed reaction of degeneration.* In such cases we cannot examine each type of fiber separately, so that the resulting mixed reaction is frequently difficult to understand, and it is quite impossible to pick out which of the fibers show a normal reaction and which a reaction of degeneration. Many instances of incomplete reaction of degeneration really belong to this variety.

Alternating Contractility.—E. Rautenberg has recently found a remarkable phenomenon of alternating contractions, *i. e.*, varying coarse and fine contractions with an equal amount of current in peripherally affected muscles (muscular atrophies and peripheral palsies) which did not show reaction of degeneration. These muscles under faradic stimulation (single interruptions and tetanizing stimulation) showed an abnormal fatigue, the contraction during frequently repeated stimulation diminished more quickly than normally, and under certain conditions disappeared entirely. Where a tetanizing stimulation was used, there appeared also a lengthening of the latent period of stimulation. This alternation of weak and strong contractions is interpreted by Rautenberg as a disturbance of contractility and analogous to the pulsus alternans of the heart. (See p. 162.) He does not discuss its diagnostic significance nor its presence in different diseases of the muscles.

Peculiar Electric Reactions of Certain Old Peripheral Palsies.—Placzek,[1] and subsequently Bernhardt,[2] have described a peculiar phenomenon which is in

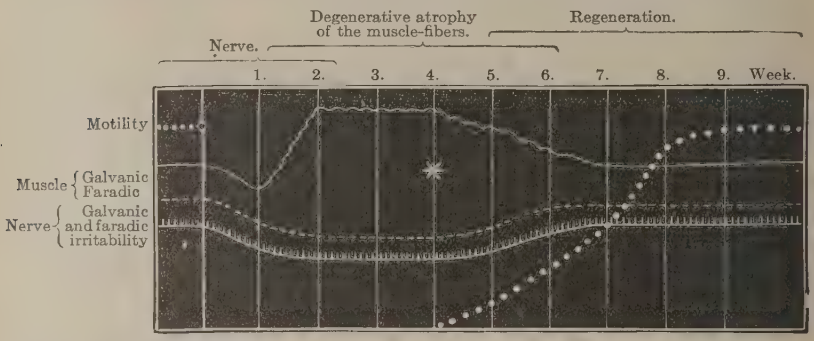


Fig. 397.—Diagram of the course of irritability in partial reaction of degeneration. See the explanation of Fig. 396. The faradic and galvanic irritability of the nerves and the faradic irritability of the muscles are only slightly diminished. Motility returns early. Compensation early and complete. Nerve degeneration probably absent.

rare cases observed as a termination of severe peripheral facial palsies. In contrast to the usual findings, the electric reactions of the nerve muscle in some of these old facial palsies reappear, although the paralysis of voluntary motion remains permanent. This phenomenon is highly interesting from a theoretic standpoint, and the author would regard it as analogous to the behavior of the so-called mild peripheral palsies, in which the paralysis of voluntary motion exists together with maintained electric excitability of the peripheral parts. Both conditions may be explained only by the supposition that changes exist in the peripheral nerves which block voluntary impulses, but do not disturb the peripheral excitability of the nerve or muscle. In the old palsies exhibiting this phenomenon there can be no doubt that peripheral regeneration has taken place, but that the blockading of voluntary impulses nevertheless permanently remains. This is difficult to understand if we cling to the old theory of the necessity of efferent irritations for the trophic integrity of the nerve muscle. This old theory, however, does not seem to obtain in all cases, since Bethe has shown that, when the union of divided nerve-fibers is prevented in young animals, a peripheral regeneration may nevertheless occur, so that the nerve-fibers regain their electric irritability. Under the conditions mentioned above, reflex impulses which maintain the muscle tonus and preserve the vitality of the nerve and muscle in the periphery, might also be conceived to

[1] Berlin. klin. Woch , 1893. [2] Ibid., 1903.

pass the obstacle. As far as the author knows, this question has not been investigated.

Myotonic Reaction (Erb).—This occurs only in Thomsen's disease (myotonia congenita). It is characterized by a peculiar persistence of the contraction after the cessation of the stimulation. The contractions are sluggish, and, when the galvanic current is steadily applied to the muscles, are often characteristically rhythmic and wave-like (galvanic myokymia). Even very weak currents will excite these phenomena (muscle hyperirritability). The anodal closure contraction (An.C.C.) of the muscle is frequently more vigorous than the cathodal closure (Ca.C.C.). Theoretically, it is of interest to know that, according to Panzini (ref. in Sem. méd., 1908, No. 15, p. 175), the muscles of new-born mammals, the normal muscles of the toad, and, furthermore, muscles poisoned by veratin, digitalin, hellebore, oxalic acid, and sodium salts give a myotonic reaction.

Neurotonic Reaction.—A few years ago Marina [1] and Remak [2] independently described a rare form of reaction which they called *neurotonic reaction*. Marina found it in *hysteria*, and Remak in a case, in all probability, of *progressive muscular atrophy*.

In this reaction, without any increase of the quantitative minimum irritability, anodal opening contraction appears very early from stimulation of the nerve, but not of the muscle. There is also a special tendency of the nerve to cathodal closure and anodal opening tetanus. The closure tetanus can be prolonged beyond the opening of the current, and the faradic tetanus of the nerve persists after stopping the stimulation. These characteristic phenomena depend essentially upon nerve irritation, and they cannot be excited by stimulation of the muscle.

Reaction in Tetany and Spasmophilia.—A quantitative increase of the electric irritability of the nerve-trunks is usually found in these conditions, although it does not affect the muscle, or, at least, not nearly to so great an extent. The quality of the reaction of the nerve is frequently, though not constantly, altered, *e. g.*, a neurotonic reaction appears with a tendency to anodal opening and cathodal closure tetanus and a prolongation of the contraction. The essential difference is that in tetany, as contrasted with neurotonic reaction proper, a quantitative increase of irritability accompanies the qualitative changes. The electric reactions of tetany are also found in the eclampsias of little children. These conditions, including spasmus glottidis, have, therefore, under the name of spasmophilia, been brought into close relationship with tetany or disturbances of the function of the parathyroids. When utilizing this reaction for the diagnosis of spasmophilia in little children, it must be remembered that, on account of the thickness of the subcutaneous fat, a stronger current must be employed for them than is usually necessary for adults.

Characteristic Reaction in Certain Traumatic Neuroses. Rumpf [3] has used the term "traumatic reaction" for this peculiar phenomenon. For some time after the cessation of a vigorous faradic stimulation the muscle will exhibit a characteristic fluctuating movement, made up of alternating fibrillary and clonic contractions (faradic myokymia). In certain cases these complex results occur even during the stimulation. Each contraction may spread from the muscle which is directly stimulated and become generalized. In these patients similar appearances are observed to follow vigorous efforts and the action of cold. (See p. 957, Fibrillary Contractions in the Healthy.)

Myasthenic Reaction.—A peculiar electric condition of the affected parts accompanies *myasthenia gravis pseudoparalytica* or *asthenic bulbar paralysis*, as the disease is usually called. It was first described by Jolly.[4] When a tetanic induction current is permitted to act upon a muscle, whether directly or through the nerve, the contraction gradually diminishes and finally disappears. This electric phenomenon is entirely analogous to the pathologic fatigue of the muscle after voluntary impulses, which is so characteristic of this disease, and it represents a higher degree of the faradic "fatigue" than can be demonstrated in health or especially in paralyzed muscles. A similar phenomenon can be elicited experimentally im muscles poisoned with protoveratrin.[5] The myasthenic reaction (diminution of contraction with increasing fatigue) is seen usually with a tetanizing current only, not with single interruptions. E. Rautenberg has recently described [6] a number

[1] See Neurol. Centralbl., 1896, No. 17. Marina's older publications upon this subject are mentioned here.
[2] Neurol. Centralbl., 1896, No. 13.
[3] Deut. med. Woch., 1890, No. 9, p. 165.
[4] Berlin. klin. Woch., 1895, vol. i, p. 2, et seq.
[5] Prognosis will be discussed separately upon p. 819, et seq.
[6] Deut. Arch. f. klin. Med., 1908, vol. xciii.

of new and interesting phenomena in myasthenia. 1. The muscle shows a remarkably sluggish reaction (myobradia) similar to the reaction of degeneration. At the commencement of the stimulation with short tetanizing currents the height of the curve increases gradually, just as in a normal muscle ("steps" of Bowditch). 2. Under continued stimulation the curve becomes progressively lower and more sluggish (true myasthenic reaction). 3. In this stage of fatigue the contractions are of unequal form and height and often of a peculiar behavior, in that the muscle becomes more and more emancipated from the stimulation, the contraction becoming at first delayed and finally quite independent of the stimulation (myautonomy). The explanation of this phenomenon is as follows: 4. The muscle is unable to respond to more frequent stimulations by superposition of contractions, as a normal muscle does, so that the number of stimulations to which it is able to respond with the regular contractions is limited by the length of the contraction; and 5. As soon as the muscle is stimulated by more than two or three short tetanizing or four or five very powerful stimulations to the second, even in the fatigue stage, it enters into a stage of irritation and contracts rhythmically. In this stage the muscle no longer shows a diminution of the contraction, a true myasthenic reaction. The contractions are, however, even more sluggish than usual. 6. In this stage the muscle has become refractory toward other, including much more powerful, stimulations. 7. The muscle having once reached this stage, sometimes a lessened or altered frequency of stimulation will suffice to maintain it in this state of irritation. One or two contractions may even take place after cessation of the stimulation, the state of irritation persisting after the stimulation. This last-named phenomenon of muscle autonomy is not identical with the myokymia, which appears in myotonia and traumatic neurosis. (See p. 1027.) It is not a muscle-wave, but a powerful rhythmic contraction of the whole muscle, with a complete emancipation of the same from the stimulation; in other words, a behavior which suggests that of the cardiac muscle. Rautenberg, in closing, points out that these phenomena are not constant in myasthenia. The author has seen the same manifestations in a case of alcoholic neuritis.

4. DIAGNOSTIC SIGNIFICANCE OF THE DIFFERENT ELECTRIC REACTIONS[1]

The myotonic, neurotonic, "traumatic," and tetany or spasmophilia reactions have been sufficiently described above, and, so far as our present knowledge goes, each is limited to its corresponding disease.

In *psychic* or *hysteric paralysis* the electric irritability remains normal. This is also a general rule for all paralyses which depend upon a lesion of the voluntary tracts above the nucleus, *i. e.*, above the gray anterior horn (*cerebral hemiplegias, transverse lesions of the spinal cord*). Sometimes, however, in these cases, especially if the paralysis has persisted for some time, the electric irritability is considerably diminished.

The condition during the first few days following a *peripheral paralysis* (see Figs. 396 and 397), and that during the entire course of the *milder forms*, will illustrate very typically a simple diminution in the electric irritability. Diminished irritability is almost invariably associated with electric exhaustibility, which is manifest by the decidedly lessened response or absence of response during a long-continued repeated stimulation to currents which at first induced vigorous contractions. When the peripheral interruption of conduction is complete, *i. e.*, when the paralysis is severe, reaction of degeneration will generally take the place of simple diminution of irritability.

Some cases of *polyneuritis* and of *lead-poisoning* furnish striking exceptions to the above statements. In some cases, instead of the expected reaction of degeneration, not only is the irritability diminished, but the diminution is so pronounced that even direct contact of the galvanic current excites no response. This proves that in these cases the muscles are affected by the toxins directly, and not alone through

[1] The electric diagnostic prognosis has a special chapter, p. 1031.

involvement of the nerve. In fact, there are many other reasons for such a hypothesis. This supposition is most probable in those cases which recover, despite a marked diminution of the direct galvanic muscular irritability. In curable cases of polyneuritis and lead-poisoning, however, the disappearance of the galvanic irritability, especially if it occur late in the disease, must be regarded as the terminal stage of R. D., and the expression of definite secondary degeneration of the muscle. (See Fig. 396 *c*, p. 1024.)

In the *myopathic forms of progressive muscular atrophy* simple diminution of electric irritability is the rule.

A simple increase of electric irritability is a comparatively rare phenomenon. It is seen in very recent neuritic paralyses and in tetany, or in that condition probably near akin to it—the so-called spasmophilia of young children. (See p. 1027.) It then depends chiefly upon nerve excitability. Increased excitability of the nerve or muscle, with coincident qualitative change, should not be confused with such a condition. (Reaction of Degeneration, Myotonic Reaction, Tetanic Reaction, see above.)

The various alterations in the reaction of degeneration (in the widest sense of the term) occur only in cases in which the muscle is affected by a break in conduction between it and its so-called trophic center[1] (situated in the nucleus, *i. e.*, in the anterior horns), or where a lesion of the center itself occurs, or where the muscle is primarily degenerated. The degeneration of the muscle, and with it the reaction of degeneration, may be absent, even when the lesion is so situated, provided it be slight and transitory. Degenerative changes in the muscle are found in all instances of reaction of degeneration, and, in fact, seem to be the physiologic expression of such a reaction. If complete, the degeneration also spreads to the nerve. A partial reaction of degeneration, on the contrary, which is observed in a moderately severe disturbance of conduction, is a sign of a degeneration of the muscle with normal, or, at most, only slightly degenerated, nerves. The retention of nerve irritability in partial reactions of degeneration seems to depend upon the preservation of the medullary sheaths.

The most frequent lesions which produce the various types of the reaction of degeneration are, therefore, *nuclear* or *peripheral paralyses*. The *spinal* and the *neuritic muscular atrophies* also often lead to partial reactions of degeneration. Yet numerous variations in the electric reactions occur in individual cases of these muscular atrophies, because in them, as contrasted with actual paralyses, each fiber is successively and, in a certain measure, individually diseased. Therefore each muscle we examine contains a series of fibers in different conditions of irritability, and the resulting reaction will depend upon whether seriously injured, slightly affected, or intact fibers predominate. In *spinal* and *neuritic muscular atrophies a mixed reaction* is the rule, whereas a *partial or complete reaction of degeneration* is much commoner in *peripheral palsies*.

Many cases, however, of spinal or neuritic muscular atrophies show absolutely no signs of reaction of degeneration as, *e. g.*, if the fibers which are seriously affected be very rapidly and quite completely destroyed, so that the reaction to stimulation actually comes from intact fibers or from those only slightly affected, and is merely quanti-

[1] See p. 1001, note 1, for the significance of the trophic character of this center.

tatively diminished. We might call this result, which is by no means uncommon in spinal and neuritic muscular atrophies, a sort of latent reaction of degeneration. The same peculiarity is presented in *bulbar paralysis*, which in its origin is identical with the *spinal form of muscular atrophy* and with the closely related *amyotrophic lateral sclerosis*. Reaction of degeneration may or may not be present. The *myopathic forms of muscular atrophy* exhibit similar variations. Although it is perfectly true that most cases exhibit no R. D., still a suggestion of such a reaction may occasionally occur even in the myopathic forms. This apparent inconsistency may depend upon the presence of many seriously affected fibers which still react to stimulation at the time of the examination. If many such fibers be present, reaction of degeneration will result; if, on the other hand, the fibers are quickly destroyed, the normal or simply diminished reaction of the unaffected fibers will persist. The occurrence of such variations (*i. e.*, reaction of degeneration in purely myopathic forms, and, conversely, its absence in spinal and neuritic forms of muscular atrophies) shows that we must not rely upon the electric examination to decide the form of the muscular atrophy, but turn to other clinical evidence, such as heredity, age, mode of extension of the disease, etc.

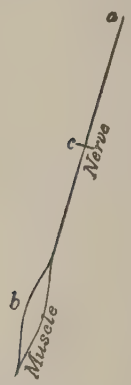


Fig. 398.

From what has been said, it is plain that it is much more important for diagnosis to demonstrate that the reaction of degeneration is present than that it is absent. A *positive reaction of degeneration* (this is perhaps the most important law in electrodiagnosis) *absolutely excludes a central or supranuclear origin* for the disease. The absence of reaction of degeneration, however, even if we except the cases where the lesion is too slight to produce it, does not always permit the exclusion of a nuclear or subnuclear cause of disease.

There is another difficulty which makes it sometimes impossible to recognize reaction of degeneration, even when the muscles are totally paralyzed from peripheral lesion. This is the greatly diminished muscular excitability, even to the galvanic current, in the late stages of the reaction of degeneration. Frequently the batteries are either too weak to excite contractions, or so strong a current is required that either the pain or the electrolytic action of the current upon the skin prevents the examination. Such an exceptionally diminished irritability should be considered for clinical purposes as practically equivalent to the reaction of degeneration. (See p. 1029, Direct Injury to the Muscles by the Toxins.)

We can sometimes utilize an electric examination to locate some obstruction to conduction in a peripheral nerve (Fig. 398). If some obstruction to the conduction, *i. e.*, some injury, occur at *c*, no contraction will result from a stimulation between *a* and *c*, but will from one between *c* and *b*. In this way the lesion can be localized at *c*, provided the nerve is accessible to examination throughout a considerable extent of its course. The test will fail, of course, if *c b* be no longer capable of being stimulated, *e. g.*, in a severe degenerative lesion where the nerve below *c* soon loses its irritability, and will be successful only in a comparatively fresh or mild paralysis in which there is at least a

partial reaction of degeneration. This condition is well illustrated by the so-called "drunkard's paralysis" or "sleep paralysis" of the musculospiral nerve, in which we can sometimes locate the injury at the point of origin of the radial nerve, because ordinarily the radial nerve can be stimulated directly above this point, *i. e.*, in the axilla, or, for the supinator longus, at Erb's point. (See note to Fig. 391.)

5. PROGNOSTIC SIGNIFICANCE OF THE ELECTRIC REACTION

Nothing could be more misleading than to base the prognosis upon the alteration in the electric reaction without at the same time heeding other facts, especially the anatomic diagnosis, *e. g.*, a rheumatic facial paralysis, even with a typical reaction of degeneration, frequently recovers; whereas a cerebral hemiplegia with perfectly normal electric reaction is often incurable. Again, a myopathic muscular atrophy with normal electric reaction is no less incurable than a spinal muscular atrophy with reaction of degeneration. Many similar instances could be mentioned.

At the same time electrodiagnosis is often of incalculable value in determining the prognosis, provided that we limit the comparison of the electric examinations to cases of the same type, and draw our conclusions only after several careful examinations repeated at considerable intervals of time. A few examples will make this evident.

Rheumatic facial paralysis, which Erb has studied so carefully in regard to the sequence of its electric reactions, supplies us with an excellent example of the prognostic value of the electric examination. If in this disease reaction of degeneration can still be demonstrated after about fourteen days, it is evident, from the diagram upon p. 1024, that at least some months, or under some conditions even as much as a year, will elapse before perfect recovery will ensue, or the case may be incurable. If after the lapse of fourteen days no more pronounced alterations of the electric excitability occur, the paralysis is slight and may recover in a few weeks. If after the lapse of fourteen days only a partial reaction of degeneration occur, we can count upon recovery in eight to nine weeks (according to the scheme, Fig. 397). If the affection be severe and associated with reaction of degeneration, a single electric examination is not sufficient to determine whether it is curable or not. We must follow the entire course of the electric changes. If after the lapse of about thirty weeks we can determine no return of the motility and no improvement in the electric irritability, or perhaps a still further impairment, the prognosis would be very grave indeed (Fig. 396 *c*). Conversely, the slightest improvement in the electric reaction, viz., an increase of the galvanic irritability in the nerve or the muscle supplied by it, or even cessation of its further depression, is of favorable significance.

The above-mentioned prognostic laws apply only to those peripheral paralyses which, like a rheumatic facial paralysis, owe their existence to a single injury, *i. e.*, whose anatomic causes neither persist nor progress. It would be obviously illogical to apply this law to other types of facial paralysis, such as a paralysis caused by a tumor or by an osteitis of the petrous bone, or even to the facial paralysis of a bulbar palsy. The distinction is that the rheumatic facial paralysis tends to recover, whereas these others tend to persist and progress.

The prognosis in a case of *infantile spinal paralysis* (poliomyelitis

acuta) is also very materially assisted by the results of an electric examination. For, just as in rheumatic facial paralysis, the cause is in operation but a short time; even in the very severe cases of poliomyelitis the cause persists and progresses for only a few weeks, and after that the disease itself is stationary. If after fourteen days to three weeks no reaction of degeneration can be detected in certain of the affected muscles, we can safely apply the same prognostic law to them that we have just mentioned for a rheumatic facial palsy. Reaction of degeneration is, however, a much more serious sign in poliomyelitis than it is in a rheumatic facial palsy, for experience has taught us that in infantile paralysis those muscles which show reaction of degeneration never recover. The reason is probably that the lesion is located in the central organs, which have little or no recuperative power.

With *lead palsy* reaction of degeneration almost always appears promptly, or, at least, a pronounced diminution of the muscular irritability to the galvanic current (see pp. 1029 and 1031) promptly results; either effect is equally significant from the prognostic standpoint. If no pronounced decrease in the electric excitability occur some time after the onset of a lead palsy, the prognosis will be favorable, just as in the rheumatic facial palsies. In lead paralysis, however, there is nothing absolutely unfavorable in the appearance of reaction of degeneration or in the pronounced diminution of electric irritability mentioned above. Only examinations repeated at considerable intervals suffice to determine the prognosis in cases of lead paralysis with reaction of degeneration. If the reaction constantly progress, the prognosis is grave; if, on the contrary, it remain the same, the prognosis is less serious; and if it evidently improve, the prognosis is favorable; for experience has taught us that when once an improvement commences in a lead paralysis, it almost always proceeds to complete recovery, and that partial recoveries are much less common. The same is found in polyneuritic and diphtheric paralyses.

We scarcely need mention that in polyneuritis there is a very decided tendency to recover just as soon as the determining causes stop; and, of course, this fact, as well as the result of electric examination, must be kept in mind in making the prognosis, which must always be determined separately for each individual muscle, and not for all those affected.

In central paralyses due to lesions in the supranuclear neurons, the results of electric examination are of less prognostic significance than in disturbances due to lesions of the peripheral neurons. For the electric irritability is not, as a rule, very much altered in these cases, even when the prognosis has from the onset been grave. However, an unfavorable prognosis should be given in disease dependent upon central lesions (cerebral hemiplegias, transverse lesions of the cord) which lead to a pronounced depression of the electric irritability, because they point to a decided secondary involvement of the peripheral motor neurons. This ill effect may be combated up to a certain point by appropriate electric treatment.

THE DEMONSTRATION OF ELECTROMOTOR EFFECTS IN THE HUMAN BODY

There are many interesting physiologic observations on the manifestations of the electromotor force in the organism during the performance of its functions. Probably the best known are the negative current vibrations set up in an

irritated nerve. Some of these may be demonstrated on the living human body, especially the currents flowing synchronously with cardiac activity (Waller), and also those currents which may be produced by muscular contractions, although these are probably due to a stimulation of the secretion of the cutaneous glands, rather than to muscular action itself. More recently, attempts have been made to employ the electric phenomenon of the cardiac activity as a physiologic and clinical method of examination in the form of an electric cardiograph, but the instruments necessary for this kind of an examination are so complicated and the examination itself is so delicate and tedious that it has so far received no general recognition. The so-called psychogalvanic reflex phenomenon has a better outlook for practical use. This phenomenon was first studied by Ferée, Tarchanow, Sticker, and Sommer, but latterly has been more carefully investigated and described by Veraguth. It consists essentially of two manifestations: If two electrodes be placed upon two areas on the body surface and a weak galvanic current, whose strength is measured by a very sensitive coil galvanometer be passed through the body, the strength of the current is found to sink at the moment when the individual receives a sensory stimulation, either because of increased resistance or because of the generation of a new opposing electromotor force, sufficient to be recorded in a galvanometer. Secondly, if the electrodes be applied to the skin without current, there appears at the time of the sensory stimulation enough current to cause a movement of the galvanometer. The psychogalvanic reflex shows a latent period of several seconds. Veraguth concludes from this that it is not really the effect of an altered contact in consequence of a reflex movement of the individual. He believes that it is probably connected with the function of the skin-glands, since he found that local poisoning of the cutaneous glands with atropin interferes with the phenomenon. This explanation agrees with the theory of physiologists, that cutaneous currents are set free by the activity of the skin-glands. (See Tigerstedt, Lehrbuch der Physiologie, 1905.) Veraguth has found that the psychogalvanic reflex phenomenon is dependent upon the intensity of the effect of the sensory stimulation. For example, an auditory impression without much effect, *i. e.* an unimportant sentence spoken to the individual, does not affect the galvanometer; on the other hand, sounds which possess a pleasant or an unpleasant effect upon the individual do. The psychogalvanic reflex phenomenon will probably attain a practical value by enabling us to control disturbances of sensibility objectively. Veraguth found that an irritation of certain cutaneous areas which are anesthetic because of a lesion of peripheral sensory nerves produces no psychogalvanic reflex, but that in hysteric anesthesias, irritation of the anesthetic parts causes this reflex to appear. This fact is all the more remarkable because the perception of the sensory irritation which is otherwise decisive for the intensity of the phenomenon is lacking in hysteric sensory disturbances, as well as in a peripheral disturbance of sensibility. The practical application of these experiments demands certain special precautionary measures which cannot be discussed here.

B. SPECIAL PART

I. EXAMINATION OF THE DIFFERENT CRANIAL NERVES

In examining the cranial nerves, the most convenient and logical plan is to take them up one after the other in their anatomic sequence. In the case of the nerves to the ocular muscles, it is, however, more practical to examine them all together, beginning with the third pair—the oculomotor.

FIRST CRANIAL NERVE; OLFACTORY

To test this nerve we employ substances with different odors, such as cologne, asafetida, oil of anise. We request the patient to smell each of them, closing first one nostril and then the other. It is convenient to test the trigeminus at the same time, employing for this purpose acetic acid and ammonia. The two sides should be tested separately. If any differences be observed, we must not attribute them to the olfactory or the trigeminus until we have convinced ourselves by a careful rhinoscopic examination that they do not depend

upon a local alteration of the mucous membrane. Disturbances of smell are very frequently due to a unilateral or bilateral inflammatory swelling of the nasal mucosa, which either injures the olfactory nerve-endings or interferes with the entrance of the odorous vapors by narrowing the nasal cavity.

Among other conditions, cerebral pressure may generally produce a paralysis of the olfactory, and, according to Huguenin, have the same significance as choked disk. A unilateral diminution of smell, provided no local cause exists in the nasal mucous membrane, appears most frequently as an accompaniment of the *hemianesthesias of hysteria* and of the *traumatic neuroses*. It is purely functional. The so-called *capsular hemianesthesia,* which depends upon lesions of the posterior part of the internal capsule, is not ordinarily associated with any disturbance of smell. (See p. 1090.) The olfactometer, constructed for physiologic examinations, has very little clinical utility, because only the gross changes, easily demonstrated without any instrument, are of any diagnostic importance.

SECOND CRANIAL NERVE; OPTIC

1. **Determination of Acuity of Central Vision.**—Snellen's, Pflüger's, or Steiger's well-known test-types are the most convenient and suitable for testing the acuity of central vision. Landolt's new vision tests are more conveniently carried about, and therefore better adapted for examining patients in bed. Errors of refraction must first be corrected. Ophthalmologic text-books must be consulted for more exact directions. We should remember, however, that even if the acuity of vision be normal, we cannot absolutely conclude the existence of pronounced changes of the retina or of the optic nerve, so that an ophthalmoscopic examination is essential (retinal hemorrhages, retinitis, choked disk, optic atrophy).

2. **Testing the Field of Vision.**—We employ the *perimeter* (Fig. 399) to determine accurately the field of vision; to demonstrate hemiopia and other visual defects (as central scotomata, quadrant defects, and quadrant anopsia); to establish the existence of unilateral or bilateral limitations of the visual field, such as accompany hysteria and other neuroses, especially the so-called traumatic neuroses, as well as to show the frequently associated fatigue of the retina. Books upon ophthalmology must be consulted for the technical application of this instrument.

We can determine the visual field approximately by a very simple procedure. The patient, with his left eye closed, sits opposite the examiner. The latter closes his right eye. The patient's right eye and the examiner's left eye are now fixed upon each other; the examiner then moves his finger in a frontal plane midway between the two eyes, from the periphery into the field of vision. He can then directly compare the patient's field of vision with his own. Of course, the distance of the finger from each eye should be exactly alike. With but one eye, it is difficult to be accurate about this distance, so that it is advisable for the examiner to orient himself by opening the closed eye from time to time. Pronounced defects in the visual field are, according to the author's experience, easily recognized by this method.

Significance of Scotomata or Defects in the Visual Field.—Dufour was the first to call attention to the great difference between "not seeing"

(vision nulle) and "seeing indistinctly" (vision obscure). If the visual defect consists of a simple lack of perception (not seeing), without obscuration of the affected areas in the visual field, the trouble must be attributed to a functional or anatomic lesion of the visual center in the cortex. Very likely the patient appreciates it for the first time during the examination. Should the patient, on the contrary, complain that the defect in the visual field does not appear to be complete,

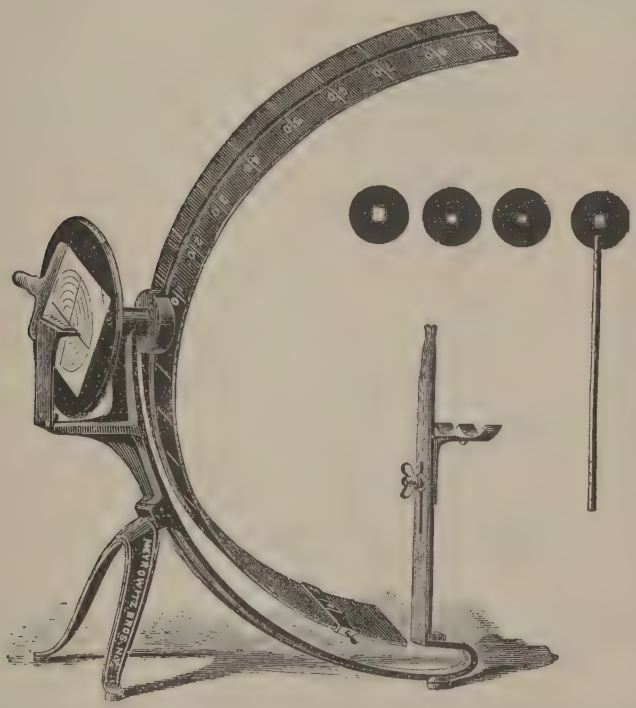


Fig. 399.—Perimeter. The examination may be made with the carrier which moves along the semicircle, or the test objects may be carried along this by means of dark disks attached to a long handle, each disk containing in its center the test object. The patient's chin is placed in the curved chin rest; the notched end of the upright bar is brought in contact with the face, directly beneath the eye to be examined, which attentively fixes upon the center of the semicircle. The other eye should be covered, preferably with a neatly adjusted bandage. The record chart is inserted at the back of the instrument, and, by means of an ivory vernier, the examiner is enabled to mark exactly with a pencil the point on the chart corresponding to the position on the semicircle at which the patient sees the test object. The various marks are then joined by a continuous line.

but merely an obscured area (in which case the patient is annoyed by this condition and is conscious of it), we should then naturally conclude that the visual center is intact, and that the visual defect depends upon some involvement of the visual conducting apparatus, either of the refracting media, the retina, the optic nerve, the optic tract, or the visual fibers. "Seeing indistinctly" is nothing more than the reaction of the intact visual centers to a faulty transmission of optical impulses; whereas "not seeing" is a consequence of the lack of visual perception of the

object in question, and naturally it occurs only in functional disturbances or anatomic lesions of the visual center. This distinction between "not seeing" and "seeing indistinctly" is of special importance in the differential diagnosis between *central* and *peripheral hemiopia.* Thus, the observation that the hemiopic scotoma in scintillating scotoma or in ophthalmic migrain is an absolute defect and not an obscuration of the visual field entirely agrees with the supposition (probable from other reasons) that the process is central and located in the cortex. (See p. 981.)

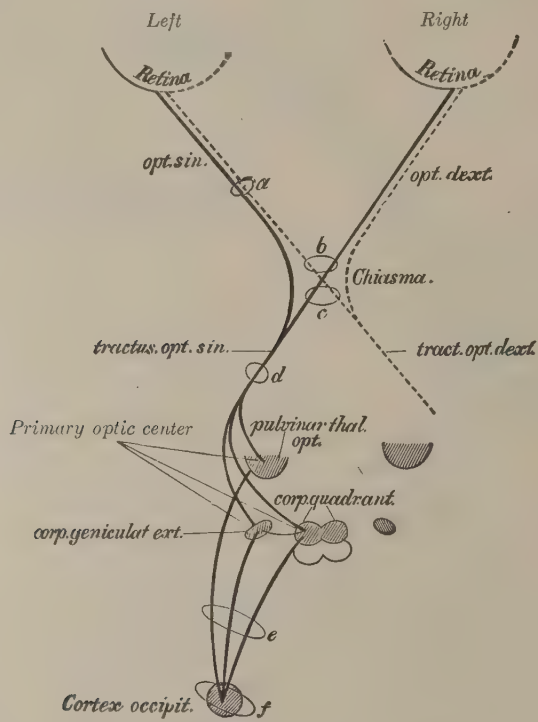


Fig. 400.—Diagram of the course of the optic fibers.

Visual Color Fields.—We are often assisted in the diagnosis of hysteric and other neurotic conditions by determining the visual color fields. These are frequently contracted and their sequence disturbed. The visual field for blue is normally the largest; but in the above affections we frequently find that other colors overlap its borders. The text-books upon eye diseases show how to determine these conditions by means of the perimeter.

Compare section 4 for the topographic diagnostic significance of defects in the field of vision.

3. **Ophthalmoscopic Examination** (see p. 907 et seq.).

4. **Topographic Diagnosis of Lesions in the Course of the Optic Fibers.**—Fig. 400 represents diagrammatically the course of

the optic fibers from the retina to the occipital lobes. The fibers arising from homonymous retinal halves form the optic tract by a semi-decussation at the chiasm. Then they proceed, in part directly, but mostly indirectly, through the so-called primary optic centers to the occipital cortex.

Without further explanation, the diagram (Fig. 400) makes it plain that a focal lesion (*a*) of the optic nerve will cause unilateral blindness; a lesion (*b* or *c*) in front or behind the chiasm will cut off the nasal halves of the retina and produce a temporal hemiopia; a lesion at *d*, *e*, or *f* will cut off both left-sided retinal halves and produce a homonymous right-sided hemiopia.

It is characteristic of the defects of the visual fields in hemiopia that the point of fixation[1] and its immediate vicinity are represented in both optic tracts, and therefore in both hemispheres, by the overlapping of fibers on the boundaries of

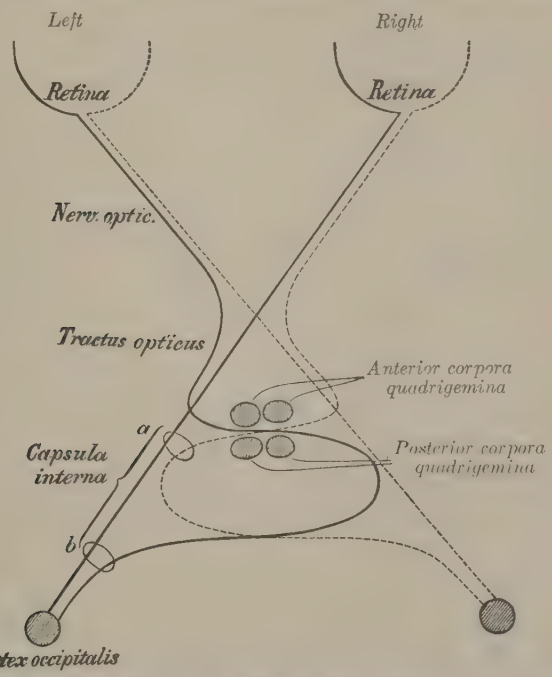


Fig. 401.—Grasset's modification of the preceding diagram: The optic fibers are depicted for simplicity sake, as if they were uninterrupted, without intercalation of the primary optic centers.

both halves of the visual fields. Consequently, in the clinical picture of hemiopia the acuity of central vision need not necessarily be impaired. In fact, the disturbance may be so slight that it is detected only by special examination; because the patient can easily displace the object images from the blind to the good half of the visual field by means of appropriate ocular movements.

Grasset has modified Fig. 400 hypothetically in Fig. 401 in order to explain the occurrence of unilateral blindness from a lesion in the extreme posterior (sensory)

[1] See Wernicke, Lehrbuch der Gehirnkrankheiten, 1881, vol. i, p. 234; ibid., Deut. Klinik, 1906, vol. vi, No. 1, Der aphasische Symptomen-complex, p. 519.

portion of the internal capsule. This condition is sometimes observed instead of a hemiopia. For the sake of simplicity the optic fibers are represented in this diagram as uninterrupted, *i. e.*, the primary optic centers are omitted. In this diagram it is assumed that the fibers which have not already crossed at the chiasm decussate between the corpora quadrigemina and then return directly to their original side; both *a* and *b* are supposed to be situated in the posterior part of the internal capsule. Hence a lesion in the internal capsule will, according to its position, produce either a crossed blindness, *i. e.*, *amblyopia* (lesion *a*) or a *homonymous hemiopia* (lesion *b*). Recent observations, however, seem to prove that lesions of the internal capsule probably do not produce hemiopic disturbances of sight. Henschen has recently examined the innervation of the different retinal quadrants, *i. e.*, the course of the visual fibers of each retinal quadrant in the trunk of the optic nerve and in the optic tracts. By dividing the retina into four quadrants by a vertical and a horizontal meridian, he found that the visual fibers of each of these quadrants run as a compact bundle in the optic fibers. This circumstance can sometimes be utilized in establishing, by aid of an exact representation of the visual field, a local diagnosis of peripheral interruptions of the visual fibers (optic atrophy, tumors).

The following diagrams from Henschen [1] illustrate this point:

5. **Detection of Simulated Unilateral Blindness.**—Unilateral blindness is quite frequently simulated. Ordinarily, we can discover it very readily by using the stereoscope. The instrument is placed in

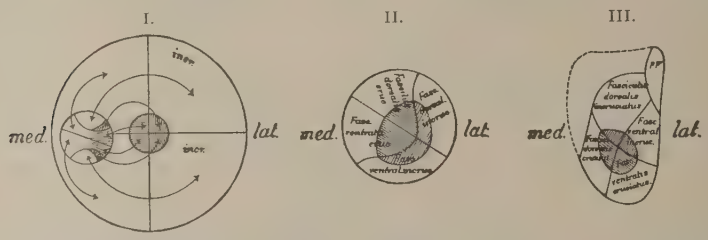


Fig. 402.—I. The four retinal quadrants: To the left is the position in cross-section of the fiber in the vascular part (anterior) of the optic nerve. The shaded parts correspond to the macula lutea, *i. e.*, the transmission of central vision. The arrows show the way the retinal quadrants correspond to the individual parts of the optic nerve. This arrangement of the fibers can be similarly made out at the part of the optic nerve which is visible to the ophthalmoscopic (optic disk) examination. *incr*, Retinal quadratus with uncrossed fibers.

II. Cross-section of the optic nerve in the non-vascular (posterior) portion. Here the macular bundles (represented by shading) lie in the center of the nerve, and the fibers corresponding to the individual retinal quadrants are arranged in quadrants about an imaginary axis running in the center of the nerve.

Explanation of the terms in the figure: The fasciculus dorsalis cruciatus corresponds to the internal superior retinal quadrant. The fasciculus ventralis cruciatus corresponds to the internal inferior retinal quadrant. The fasciculus dorsalis incruciatus corresponds to the external superior retinal quadrant. The fasciculus ventralis incruciatus corresponds to the external inferior retinal quadrant.

The figure also shows that the quadrant arrangement is retained in the non-vascular part of the optic nerve, *i. e.*, by imagining the quadrant picture of the retina seen from in front (1) with the upper end of the vertical meridian rotated outward about 45°.

III. Cross-section of the posterior part of the optic tract: *P. F.*, Fibers of the pupillary reflex (see Fig. 413, p. 1054). Other abbreviations have the same meaning as in II. The four quadrant bundles are bound together again, but still distinct. They surround the shaded bundle in the center, which corresponds to the tract of the macular fibers. The arrangement of the quadrant bundles in III. is very similar to that in the cross-section II., except that the pupillary fibers do not appear in the latter.

front of the two eyes; different letters are arranged so as not to coincide in stereoscopic union. The patient cannot recognize to which eye the individual pictures belong. If, now, he simulate a one-sided blindness, the simulation is evident, because he reads the characters which could be seen only by the supposedly blind eye quite as well as the other.

This outcome of the test does not, however, prove malingering in hysteria, because there are cases of unilateral hysteric blindness in

[1] See Salomonsohn, Deut. med. Woch., 1900, No. xlii, p. 677.

which the disturbance is shown solely during monocular vision. For the test to be free from objections, due care must be exercised that the patient obtains no information by alternate opening and closing of a single eye or by moving the picture. Appropriate stereoscopic pictures for such an examination with the stereoscope will be found at the end of Dr. M. Burchardt's treatise, "Practical Diagnosis of Simulation" (Berlin, Enslin, 1891).

THIRD, FOURTH, SIXTH CRANIAL NERVES; THE OCULAR MUSCLES; NERVES, INCLUDING THE SYMPATHETIC MOTOR INNERVATION OF THE EYE REGION

1. Functions of the External Ocular Muscles

The *third cranial nerve* (oculomotor) supplies the following muscles: Levator palpebræ superior, rectus superior, rectus inferior, rectus internus, and obliquus inferior, the pupillary sphincter, and the muscles of accommodation (both the latter from the short branch of the ciliary ganglion).

The *fourth cranial nerve* (trochlear) supplies the superior oblique (trochlearis) muscle.

The *sixth cranial nerve* (abducens) supplies the external rectus muscle.

The muscles which move the eyeball have the following functions:

I. Internal rectus: movement of the eyes inward without any meridian inclination.

II. External rectus: movement outward without meridian inclination.

III. Superior rectus: movement upward and inward with rotation of the upper extremity of the vertical meridian inward.

IV. Inferior oblique: movement upward and outward with rotation of the upper extremity of the vertical meridian outward.

V. Inferior rectus: movement downward and inward with rotation of the upper extremity of the vertical meridian outward.

VI. Superior oblique: movement downward and outward with rotation of the upper extremity of the vertical meridian inward.

The external and internal recti suffice for directing the eyes in the horizontal axis, but movement in the vertical axis (upward and downward) requires the joint action of one rectus and one oblique. The inferior oblique belongs to the superior rectus and the superior oblique to the inferior rectus. The principal function of the obliques is, therefore, to limit the tendency to inward movements and to rotation of the eye in the frontal plane, which would take place without their action. Any vision directed obliquely between the vertical and the horizontal axes necessitates the joint action of three different muscles. One of them acts to prevent rotation in a frontal plane.

2. Paralysis of the Muscles which Move the Eyeball

The disturbance of function which may result from a paralysis of the eye muscles can be essentially determined from the preceding description of their function. If one or more muscles of the eye be paralyzed, the eye will remain immobile when an attempt is made to turn it in the direction ordinarily accomplished by the muscles affected. To demonstrate the existence of a paralysis of the eye muscles, the patient should follow with his eyes (but with the head absolutely

fixed) the movement of the examiner's finger in every direction, while the examiner compares the excursions of the two eyes. This is easily accomplished by observing the position of the corneal margin in relation to the angle of the eye, a procedure generally sufficient for a hasty test. A slight paresis may, however, be hidden by the tendency such a patient has to fuse the double images. Therefore, in any doubtful case, it is well to test each eye alone, covering the other eye. A slight weakness will sometimes be disclosed by having the patient attempt the extreme positions, and then observing either that the position cannot be retained for any length of time or, else that it produces an accompanying tremor of the globe (nystagmus, see p. 1050), although the weakness is not sufficient to diminish the extent of the excursions. In testing the internal recti we must especially note their behavior in attempted convergence of the eye. (See p. 1049.)

In complicated muscular paralyses of the eyes it is often difficult to form a judgment as to the function of the oblique muscles, because they are in such intimate association with the recti. In such a case, and especially in distinguishing the more delicate disturbance of the eye movements, testing the torsion of the eyeball is especially significant. If the eyeball move normally, no axial deviations occur, because the tendency to such deviations common to all the eye muscles, excepting the external and internal recti (p. 1037), is counteracted by the associated action of the other muscles. Just as soon as this extremely finely balanced associated action of the eye muscles is injured by the paralysis of such muscles as possess axial deviating components, axial deviations of the eyeball must ensue. The demonstration of such axial deviations or movements of rotation in a definite visual direction, and the determination of the muscles which are responsible, permits conclusions in regard to the finer defects of movement. These cannot be made out in an examination of the gross excursions of the eyeballs, for in complicated paralyses it is especially difficult to recognize the functions of the obliques in the movements of the eyeball, because the direction in which these muscles pull is affected by the action of the two recti muscles. In order to draw diagnostic conclusions concerning rotation it is only necessary to keep in mind that rotation with an inclination of the upper extremity of the vertical meridian inward depends upon the superior rectus and the superior oblique, while the reverse rotation depends upon the inferior rectus and the inferior oblique. If a rotation occur in any individual movement of the eye, we naturally infer that the fault depends upon the muscle, which by its help should prevent such rotation, and which, unaided and unopposed, would accomplish the opposite rotation. We test rotation by having the patient look upward and outward, and then downward and outward.[1] While looking upward and outward, rotation of the right eye in the direction of the hands of a clock (as seen by the examiner) signifies paresis of the inferior oblique and preservation of the superior rectus; while looking downward and outward, a similar rotation signifies paresis of the inferior rectus with intact superior oblique.

More pronounced paralyses of the eye muscles are also evidenced by strabismus (*paralytic squinting, paralytic strabismus*). Paralytic strabismus can be differentiated from concomitant strabismus by the fact that in the former a deviation of the eyeball from the normal reciprocal

[1] Or if these movements cannot be carried out, having him make the attempt.

position shifts with the direction of vision, whereas in concomitant strabismus it remains the same in every direction of vision.

Patients with paralyses of the eye muscles ordinarily complain of double vision; hence the existence of diplopia and its peculiarities may be utilized for diagnosis. For this purpose it is essential to know to which eye each one of the double pictures belongs. This is determined most readily by putting before the patient's eyes differently colored glasses, which may be conveniently slipped into the spectacle frame used by ophthalmologists. From the patient's statements as to the color of the pictures it is easy to determine the eye to which each of the double pictures belongs. In some cases, especially in old paralyses, double vision is first discovered by making use of these colored glasses, whereas without this device patients disregard one of the pictures, *i. e.*, they no longer see it. It is quite possible, without the colored glasses, to determine to which eye each of the double pictures belongs, by covering one of the patient's eyes, and then having him say which of the pictures disappears. In paralyses of the eye muscles which act horizontally, the double pictures will stand side by side. These we call *crossed double pictures* (*crossed double vision*), if the picture lying to the left (from the patient) belong to the right eye. On the contrary, we speak of *homonymous* or *non-crossed double pictures*, if the left picture belong to the left eye. In accordance with well-known physiologic laws of projection, the appreciated picture—that is, the projection of the retinal picture in space—seems to be inverted. Hence *homonymous* or *non-crossed double pictures* depend upon a crossing of the visual axis in front of the object, *i. e.*, upon convergence; or, in other words, upon abducens paralysis. On the contrary, *non-homonymous* or *crossed double pictures* depend upon divergence of the visual axes, *i. e.*, paralysis of one or both internal recti. The following laws of double vision are applicable for diagnostic use. They depend upon the fact that the projection of the retinal pictures in space seems to shift in a direction opposite to the movements of the eye.

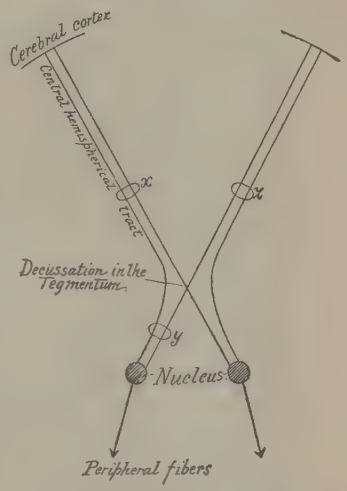


Fig. 403.—Diagram of the bilateral central innervation of the nerves to the eye muscles and most of the remaining motor cranial nerves. The lesion x causes no evident paralysis, because the tracts of the opposite side remain intact; the lesion y would, however, and so would lesions x and z together. Coexisting lesions in the latter places (x and z) cause so-called bulbar paralysis (p. 1090).

(1) That eye is paralyzed whose image appears to be deviated from that of the other in any one direction of vision; and (2) the paralysis involves the muscle or muscles which move the eyeball in the same direction in which the deviated object seems to shift when the line of vision is altered.

In examining for double vision it is useful to know that some cases see double only when objects are at a considerable distance from the eye: perhaps because the effort of accommodation in focusing at a near distance makes it easier to disregard the second indefinite picture. It is also important to remember that double pictures separated but little from one another are frequently not recognized as such by the patient, but are described by him as "blurred" (*i. e.*, obscure) vision. Closing one eye improves the patient's vision in this type of disturbance.

Besides double vision, patients with paralysis of the eye muscles very frequently complain of *vertigo* (ocular vertigo), and *disturbance of equilibrium* in walking and standing. (See pp. 1093 and 961.) This is psychic and depends upon the disturbances of orientation in space. According to the author's experience, ocular vertigo depends principally upon paralysis of the ocular muscles which rotate the eyeballs; whereas mere paralysis of the abducens and internal recti ordinarily causes little or no vertigo. This is comprehensible without further explanation; for, despite the diplopia, the patient with these latter paralyses sees objects at least in normal vertical orientation; whereas in paralysis leading to rotation, objects appear upside down.

Ocular vertigo differs from other kinds of vertigo, inasmuch as it disappears upon closing the eyes.

If the paralysis be simple, and especially if it be unilateral, the diagnostic laws concerning the significance of the kind of double pictures mentioned above easily lead to a diagnosis; but in complicated binocular paralysis the recognition of the paralyzed muscles from the double pictures alone is often very difficult. Here one of the most reliable methods is to determine the fields of vision by means of the *perimeter*. It is merely an improved method of testing the excursions of the eyeball in various directions, and is accomplished by fixing the head by means

Fig. 404.—Unilateral ptosis (New York City Hospital).

of the perimeter, and estimating those points in the instrument which can be directly (centrally) seen, *i. e.*, at which fine type can still be read. The projection fields may be recorded on charts just as the visual fields.

Monocular double vision, which is not uncommon in hysteria, must not be confused with binocular diplopia occasioned by paralyses of the muscles of the eye. The former is often attributed to a partial spasm of the ciliary muscle, in consequence of which a portion of the lens acts as a prism and throws a second picture upon the retina. This theory is probably incorrect, for certainly it will not apply to many cases; in those which the author himself has observed the monocular diplopia was evidently a purely psychic phenomenon. Monocular diplopia is, therefore, a stigma

of hysteria, and it is important to bear this in mind in any instance of double vision, before making a diagnosis of ocular muscle paralysis, which causes only binocular diplopia.

The diagnostic importance of ocular muscle paralysis is very considerable, because experience has shown that it almost always depends upon a lesion of the peripheral motor neurons (*i. e.*, the subnuclear fibers or the nuclear region itself) and practically never upon a supranuclear lesion, or a lesion of the central fibers. As each one of the ocular nerve-muscles must possess a central tract running to the cortex, this peculiarity demands explanation. This may be given by the supposition that the nuclei of the ocular muscles are innervated not by one, but by both hemispheres. Fig. 403 readily explains why a lesion in one hemisphere, even if it destroy the central fibers, causes no apparent paralysis of the corresponding eye muscle, although a portion of

Fig. 405.—Bilateral ptosis, normal position (Neurologic Department, Massachusetts General Hospital).

the innervation for both sides is affected, the intact hemisphere apparently furnishes sufficient innervation for both sides. Therefore, since there is no method of measuring the absolute power of the muscles, the bilateral defect of innervation escapes observation. This is also difficult in the case of the other cranial nerves where analogous conditions exist. When the lesion, even though small, occurs at *y*, in the region of the nucleus or below it, all the fibers are interrupted. Still another circumstance may aid in preventing the occurrence of a muscle paralysis in unilateral supranuclear lesions of the hemisphere; it is possible that the central fibers do not run so compactly as is represented in the figure, but are distributed over different points of the cortex, so that a circumscribed lesion could not very easily destroy many of them. In favor of this is the fact that Beevor and Horsley, in their experiments on the internal capsule of apes were able to cause conjugate lateral movements

of both eyes (rectus internus and contralateral rectus externus) only. (See Fig. 427, p. 1097, irritation points of the internal capsule.)

Fig. 406.—Bilateral ptosis, showing effort to open eye, using muscle of forehead (Neurologic Department, Massachusetts General Hospital).

On the other hand, in bilateral hemispheric lesions or in excessive superficial affections of the two sides of the brain (meningitis, etc.), bilateral ocular muscle

Fig. 407.—Bilateral ptosis, showing effort to open mouth (Neurologic Department, Massachusetts General Hospital).

paralyses may occur as "pseudobulbar" paralyses (p. 1090). The few examples in which, with unilateral cortical lesions, contrary to ordinary experience, isolated

crossed ocular muscle paralyses (especially ptosis) have been discovered are explained by assuming that in many individuals the bilateral hemispheric innervation is insufficiently developed, or that the central fibers are more compact and localized. In one of these cases that part of the frontal lobe adjacent to the middle portion of the anterior central convolution was found to be involved, and in the other cases the parietal lobe. The first corresponds to localization of the center for conjugate ocular movements. (See p. 1046, Fig. 424, p. 1095.) The latter is probably due to a lesion of the association fibers connecting the center for optic perception with the center for ocular movements (see p. 1046); this causes a disturbance of ocular motility because of the loss of physiologic innervation. Isolated ptosis of central origin has been found only in lesions of the parietal lobe. This will be discussed upon p. 1046 along with the localization of the center for conjugate ocular movements. (See Fig. 424, p. 1095.)

In paralyses of the ocular muscles one can, therefore, generally exclude supranuclear causes, so that a diagnosis of the situation of the lesion is for the most part limited to a distinction between a nuclear and a subnuclear type. This differentiation in the case of the oculomotor is frequently simple, because in subnuclear (*i. e.*, entirely peripheral) paralysis the nerve is affected almost always in toto, whereas in nuclear paralyses the separate functions of the nerve can be affected, so to speak, individually, since the oculomotor nucleus is anatomically situated in functionally different areas. Especially characteristic for most nuclear paralyses is the preservation of the pupillary and accommodation fibers of the oculomotor. The following plan, copied from Kahler and Pick, presents the anatomic arrangement of the different parts of the oculomotor nucleus and their relation to the neighboring trochlear nuclei. Its study will facilitate a more exact local diagnosis in nuclear paralyses.

Anatomic Arrangement of the Different Components of the Oculomotor Nucleus.

[Anterior (proximal).]
1. Accommodation.
2. Sphincter iridis.

Median. { 3. Rectus internus. / 4. Rectus inferior. } Lateral. { 5. Levator palpebræ superioris. / 6. Rectus superior. / 7. Obliquus inferior. }

Trochlearis.

[Posterior (distal).]

3. Ptosis, Including So-called Sympathetic Ptosis

By ptosis is meant a paralytic drooping of the upper eyelid so that the lid covers the eyeball more or less completely and thereby narrows the palpebral fissure. Ptosis ordinarily results from paralysis of the levator palpebræ superioris, supplied by the oculomotor. (See below, Sympathetic Ptosis.) In this connection it is necessary to differentiate paralytic ptosis from a spasmodic condition of the orbicularis palpebrarum, by which the upper lid is drawn down over the eye and the palpebral fissure narrowed. The distinction is usually easy. In the former, paralytic or true ptosis, the excursion of the upper lid upward, is diminished if not entirely prevented; whereas in a spasm of the orbicularis this need not be the case, because unless the spasm be too strong, the levator is able to overcome the tonus of the orbicularis. In a spasm of the orbicularis, moreover, the wrinkles about the eye are ordinarily more prominent, and the eyebrow is placed lower than upon the normal side; whereas in paralytic ptosis the eyebrow, by means of its innervation

by the facial, seems instinctively elevated higher than normal to counterbalance the defect.

The so-called *sympathetic ptosis*, which was first described by Horner in 1869, must not be confused with ptosis due to paralysis of the levator palpebræ. Here, although the lid aperture of the affected side is narrower than upon the healthy side, and its upper lid hangs lower, it can be demonstrated that the excursions of the levator palpebræ are in no way diminished; but the eyeball often seems sunken into the orbital cavity, the pupil is ordinarily somewhat narrowed, and frequently abnormalities of the sweat secretion and of the vascular innervation appear upon the affected side of the face. This symptom-complex depends upon a paralysis of the so-called Müller muscle (supplied by the sympathetic), comprising the smooth muscle fibers of the superior oblique, inferior oblique, and orbitalis. Stimulation of the two former widens the lid aperture; stimulation of the latter projects the eyeball somewhat forward from the orbit. A paralysis of these fibers causes an appearance of the eyes diametrically opposite to that in Graves' disease (exophthalmos) (Gräfe's symptoms, see p. 1050). This latter symptom is to be attributed to an irritation of these smooth muscles.

Congenital ptosis, which is not very rare, is partly sympathetic in nature, and partly dependent upon a congenital (nuclear) paralysis of the levator palpebræ superioris. Concerning isolated ptosis in lesions of the parietal lobe see p. 1045.

4. Conjugate Paralyses and Conjugate Deviation of the Eyes

The so-called conjugate eye paralysis will be discovered in a binocular examination for the mobility of the eyes (described above) by means of fixation upon the finger held in front. It occurs in cerebral diseases, and

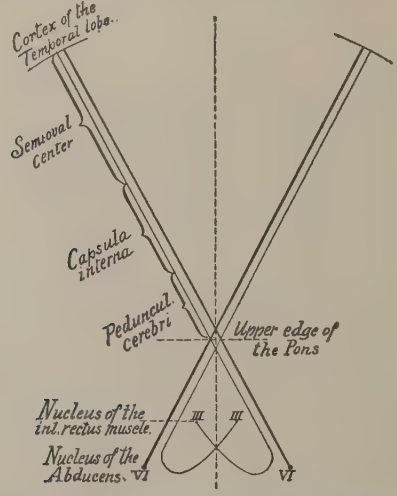


Fig. 408.—Diagram of the tract for the associated lateral movements of the eyes. The upper half of the diagram, as far as the decussation (at upper edge of the pons), is to be regarded as a frontal section; the lower half of the diagram (the pons), as a horizontal section through the brain. The heavier of the two pairs of lines which intersect each other represents the central tract of the abducens; the lighter, the central tract of the internal rectus of the opposite side.

consists of weak, deficient, or absent mobility of the two eyes to the same side. These conjugate paralyses are usually due to a lesion situated in a tract which apparently runs from the middle portion of the frontal lobe, adjacent to the anterior central convolution, to the nucleus

of the abducens of the opposite side and to the nucleus of the rectus internus of the same side. The cortical center of this tract lies, together with the center for the rotation of the head to the opposite side, in the foot of the middle frontal convolution,[1] *i. e.*, the area bordering on the central convolutions. They may probably also be due to a lesion in a fasciculus which is situated in the infraparietal lobe and connects the center for ocular movement with the center of the optic nerve (Landouzy and Wernicke). A conjugate paralysis of the lateral ocular movements due to a lesion of this area may be reconciled with the theory that the real motor center for the movements lies in the frontal lobe (see above) if we assume that, in consequence of the close association of the visual sphere of one hemisphere with the ocular movements toward the opposite side, one that is quite inseparable from the usual visual act, a second innervation comes from the visual area during voluntary lateral projection. A paresis of the conjugate lateral ocular

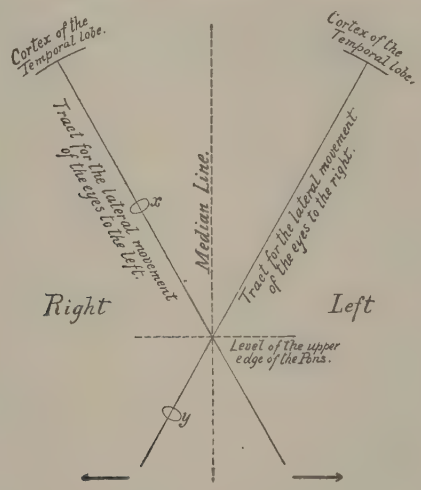


Fig. 409.—The same diagram simplified.

movements starting from this point of connection may cause the loss of this second innervation current. Fig. 408 is a schematic representation of the course of this tract based upon pathologic findings (Leichtenstern-Hunnius). It will be seen that the fibers for the rectus internus, instead of passing directly to this nucleus, take a circuitous course through the region of the opposite abducens nucleus, and that the entire tract decussates in the anterior half of the pons.

In order to explain the way in which this tract can be affected by cerebral lesions at different locations, it is best to simplify the diagram, as in Fig. 409. The arrows mean that the tract proceeding from the cortex of the left hemisphere supplies the lateral movements of the eyes to the right; the tract from the opposite side, those to the left. With

[1] See author's monograph, Beitrag zur corticalen Localization der conjugierten Seitwärtsbewegungen der Augen und des Kopfes, Deut. Arch. f. klin. Med., 1905, Bd. lxxxvi.

this explanation it is easy to understand that a lesion (x) above the pons will prevent the movements of the eyes to the side opposite the lesion, while, on the contrary, a lesion (y) below the upper edge of the pons will paralyze the movements of the eyes to the same side as the lesion.

Since conjugate paralyses are ordinarily combined with a conjugate deviation of both eyes to the side of the non-paralyzed antagonists, with a lesion x (Fig. 409) an ocular deviation to the right will be noted, and with a lesion y, one to the left. Briefly, in lesions above the pons the patient looks toward his cerebral lesion; whereas in lesions of the pons and below the pons, he looks away from it.

Conjugate paralysis with deviation of the eyes occurs principally as a symptom of hemiplegia in acute cerebral lesions (hemorrhage, softening). Like hemiplegic paralyses of the extremities, it is frequently an indirect focal symptom, depending upon lesions located at various points,

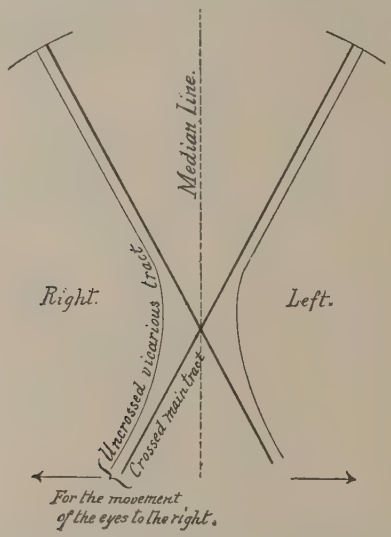


Fig. 410.—The same diagram modified to include the uncrossed vicarious innervation.

and generally soon disappears with the subsidence of the remote action. In some cases, however, the persistence of the hemiplegia proves that the entire unilateral voluntary tract is destroyed, and with it the accompanying conjugate ocular tract (see Fig. 427, p. 1097, irritation points of the internal capsule), running through the internal capsule, and yet the conjugate ocular paralysis gradually disappears. We are compelled to assume, therefore, that, although most of the tract decussates, there must exist in the other hemisphere an uncrossed tract, possessed of the same function, which in apoplexy is affected more or less strongly by the remote action, but which, after the subsidence of the apoplexy, can take the place of the affected crossed tract. The ocular movement toward the same and opposite sides as a result of stimulation of the internal capsule (see Fig. 427, p. 1097, experiments of Beevor and Horsley on apes) furnish direct experimental proof of the theory

of bilateral innervation of the conjugate movements of the eyes. Fig. 409 must, therefore, be modified in accordance with this theory, as in Fig. 410. Naturally, it may also be inferred that the vicarious action of the healthy hemisphere can be improved by constant use.

Besides being due to paralysis, conjugate deviation of the eyes may result from spasmodic action. This cause may be assumed when we note the existence of similar spasms in other muscles upon the side of the deviation. The local diagnostic conclusions from the direction of the deviation are then naturally simply reversed.

5. Paralysis and Weakness of Converging Movements of the Eyes

Convergence of the eyeballs requisite for binocular vision of near objects is naturally affected or rendered impossible by paralysis of one or both internal recti. Peculiar conditions occur, however, in which the internal recti functionate normally

Fig. 411.—Exophthalmic goiter, showing exophthalmos and goiter (Dr. J. J. Putnam, Massachusetts General Hospital).

for all conjugate lateral movements of the eyes, but not for converging movements. Such observations have led to the assumption of a separate convergence center probably located in the pons. Its existence, however, is still problematic, because isolated convergence paralysis could quite as well depend upon the paralysis of a special tract supplying each internal rectus as upon the lesion of a center. A lesion of a central tract (*i. e.*, a supranuclear oculomotor and probably a bilateral convergence tract), different from the tract of the conjugate movements of the eyes (Fig. 408), would explain the peculiarity. The one thing which seems to be certain

(and this was confirmed by one of the author's autopsies upon a tumor of the pons) is that convergence can be paralyzed by a lesion of the pons, while the other movements (conjugate, see p. 1046 et seq.) of the internal recti remain intact. In this sense the symptoms can be utilized for local diagnosis.

In addition to the characteristic and complete paralysis, a mere weakness and insufficiency of convergence may be of considerable diagnostic importance in neurasthenic states and in exophthalmic goiter. In the latter this phenomenon is called *Möbius's symptom.* Insufficiency of convergence, which occurs also in myopia, is experienced subjectively by the appearance of the so-called asthenopic difficulties, by a sense of fatigue, by obscure and double vision when the eye is steadily accommodated for near objects, and, on the other hand, objectively confirmed by the exhibition of latent external strabismus for near vision. This latent external strabismus appears when the binocular focusing power fails, and can be demonstrated by fixing the glance upon a near object (*e. g.*, 25 cm. distant) and then suddenly covering one eye with the hand. With insufficient convergence the covered eye will noticeably deflect outward, since the effort for convergence has become unnecessary. Conversely, the patient may also fix a nearby object while one eye is screened and then suddenly uncovered. In this case the eye previously covered and deflected turns inward for the purpose of binocular fixation. In spite of such subjective and objective confirmation of insufficiency of convergence, the degree of convergence which is transitorily accomplished by vigorous voluntary impulse is in such cases oftentimes considerable, so that, according to the author's experience, the Landolt ophthalmodynamometer (which measures the convergence attainable by the maximum voluntary effort) does not suffice to demonstrate the insufficiency in exophthalmic goiter.

6. Nystagmus

In examination of the eyes one must always be on the lookout for nystagmus, by which is understood a rhythmic oscillation of the eyeball, especially marked when the eyes are in an extreme position. It is much more commonly a lateral than a vertical movement. It is generally an intention tremor. (See p. 951.) It is frequently associated with paralysis of the eye muscles (see p. 1039), and with many other affections of the eye and of the brain, most commonly, however, multiple sclerosis. The neurodiagnostic importance of nystagmus is limited, because it occurs in all sorts of ophthalmologic affections, especially in those which early in life cause markedly defective vision, *e. g.*, in corneal opacity, in cataract, either congenital or early acquired, in congenital iridochoroiditis and retinitis pigmentosa, in coloboma of the choroid and of the retina, and finally in albinism. [Oftener than true nystagmus in these last-named conditions, we encounter irregular twitching movements of the eyeballs, to which the designation nystagmoid movements is given.—Ed.]

7. Contractions of the Ocular Muscles

A contraction of certain of the external ocular muscles, evidenced by anomalous positions of the eyeball, plays a part of some importance in hysteria. These positions change so constantly that it is impossible to confuse them with paralyses or with concomitant strabismus; besides, in hysteria, as contrasted with the latter condition, a voluntary movement fails to alter to any considerable extent, if at all, the position of the deviated eye in relation to the palpebral fissure. The history will generally aid in any doubtful case. A differential diagnosis between spasm and paralysis might be difficult in some instances unless the presence of contracture in an adjoining muscle (facial spasm, blepharospasm) should decide the question.

(See p. 1049 in regard to conjugate deviation of both eyes due to spasm.)

The so-called "Gräfe's sign," which occurs in exophthalmic goiter, is probably to be regarded as a spasmodic contracture of the sympathetic superior oblique muscle (p. 1046). This sign gives the patient with exophthalmic goiter a very characteristic expression, and is of con-

siderable diagnostic importance. It is elicted by having the patient look down gradually; as the eyeball lowers it is noticed that the upper lid does not follow the movement of the eyeball, but either remains still or moves only slightly, thus exposing a more or less broad band of sclera between the cornea and the upper lid. [This sign is not limited to Grave's disease, but may be seen in other diseases. Barker and Hanes[1] have published a series of 33 cases of chronic nephritis, 16 of which showed marked exophthalmos with von Gräfe's sign. They believe it to be the result of irritation of the autonomic sympathetic fibers. This causes contraction of Landström's muscular cuff or opponens recti.—Ed.] For its demonstration it is important to avoid a dazzling light, because, apparently for protection, this seems to furnish sufficient stimulus to enable a patient to overcome the phenomenon. Gräfe's symptom may be easily simulated, in which case the action of the levator palpebræ superior preponderates over that of the smooth tarsal muscle.

8. The Pupillary Phenomena

Diagnostically, these are of the greatest importance.

Diameter of the Pupils.—The size of the pupils can only be estimated in regard to the illumination. It is best to observe them in illumination of medium intensity. In doubtful cases we should compare the pupils of the patient with those of a healthy man, of about the same age, in the same light.

Schirmer[2] found that the diameter of the pupil under physiologic conditions varies greatly in different individuals, and especially at different ages. In any individual case, however, the diameter is constant for wide ranges of illumination (from 100 to 1100 meter-candles), provided that the observation be made after the eye has fully adapted itself to the particular illumination, as it does within a few minutes. If we bear this fact in mind in estimating the diameter of the pupil, we are, to a certain extent, independent of the existing degree of illumination. This diameter of the pupil, determined several minutes after full adaptation, must consequently be employed as a basis for the recognition of pathologic variations. Schirmer obtains the necessary degree of illumination of 100 to 1100 meter-candles by placing the patient within one meter of a window which is well illuminated by the sun, and yet not exposed to direct sunlight. The pupillary diameter is then determined while the patient relaxes his accommodation and convergence by looking at some distant object. Schirmer states that the observation should not be made when passing clouds are present, since the illumination will vary and may be less than 100 meter-candles. Tange found by observing these conditions that the pupillary diameter varied between 2 and 4 mm., being dependent upon age, refraction, and sex, and that in the great majority of cases it was between 2.5 and 3 mm. In advanced life the pupil is usually smaller than in youth.

Narrowing of the pupil (*miosis*) is found physiologically during sleep and old age, pathologically as an early symptom in *tabes dorsalis* and in *progressive paralysis*. Eserin, pilocarpin, opium, morphin, and chloroform (the latter in pronounced narcosis) narrow the pupil. Sympathetic miosis from lesions of the (pupillary) dilating fibres of the cervical sympathetic, from disease or the sympathetic itself or of the oculopupillary fibers connecting the sympathetic nerve with the first dorsal segment of the spinal cord, is of local diagnostic importance.

Dilatation of the pupil (mydriasis) occurs in complete loss of conscious-

[1] Amer. Jour. Med. Sci., Oct., 1909.
[2] Deut. med. Woch., 1902, No. 13.

ness, in severe pain, in dyspnea, in peripheral blindness (especially from optic atrophy and glaucoma), in general oculomotor paralysis, and in some cases of tabes dorsalis and progressive paralysis. Atropin, duboisin, cocain, chloroform (in the early stages of narcosis) dilate the pupil. Children, as a rule, have dilated pupils.

W. Riegel[1] describes, as a sign of neurasthenia, under the name of "alternating mydriasis," a dilatation appearing sometimes in one, sometimes in the other, eye with a normal reaction to light.

E. Redlich has described a pupillary phenomenon in hysteric individuals. It consists of a dilatation of the pupil (irresponsive to light, but reacting to accommodation) during a cry, powerful muscular action, or hysteric attacks. He refers this to an irritation of the sympathetic, and is of opinion that the phenomenon will explain the loss of pupillary response in many cases of hysteria, and that voluntary dilatation of the pupil is often due to a similar mechanism. There is the possibility, however, that in hysteria the dilatation and loss of pupillary reaction are due to the direct influence of the cortex upon the pupil. This has been proved in Haab's cortical pupillary reflex. (See p. 1059.) The loss of pupillary reaction during epileptic attacks and in meningitis is likewise in favor of a cortical pupillary rigidity, considering the localization of the causal process.

Irregularity in shape of the pupils may, of course, occur in diseases of the nervous system, but in most cases it depends upon some local disease in the neighborhood of the pupil (synechia). [One should guard against mistaking an irregular distribution of black pigment at the pupillary margin for irregularity of the pupil itself.—Ed.]

Inequality of the pupils is rare in health, and when present, most frequently depends upon an unequal refraction of the two eyes. It is not uncommon in the various unilateral cerebral affections, in progressive paralysis, in tabes dorsalis, in unilateral disease of the sympathetic, of the oculomotor, or of the optic nerve, and in migraine attacks. An inequality of the pupils is fairly common in neurasthenia, and is then usually of a vacillating character ("alternating mydriasis") (see above).

See p. 1058 et seq. concerning an inequality of the pupils which depends upon the loss of reaction and dilatation of one pupil.

On account of the *crossed pupillary reaction* (see below) both pupils are equally contracted when only one is exposed to light. Yet, not rarely, persons are observed in whom the pupil adjacent to the source of light is narrower than the shaded pupil. Too little attention is paid to the diagnostic significance of this phenomenon. It may be that it is a stigma of neurasthenia.

Anomalies of Pupillary Contraction.—*Pupillary Light Reflex.*—Exposure of the pupil to illumination narrows not only the pupil of the same side, but also the pupil of the other eye, thus giving rise to a direct and a crossed-light reflex or reaction. The part of the oculomotor nucleus (iris nucleus, see p. 1045) which innervates the iris must be considered as the center of this reflex.

A convenient method of testing the reaction of the pupils to light is as follows: With a moderate illumination (candle light) in front of the patient's face we alternately expose and then shade one eye with the hand, watching the effect of the light upon that pupil and upon the other pupil; then we do the same thing to the other eye. If the test with a moderate light does not produce the pupillary contraction, the examination should be repeated with a dazzling light (sunlight, an illumination lens, or a concave mirror).

[1] Zeit. f. Nervenheilk., 1900, vol. xvii, p. 169.

This customary procedure for the exact quantitative estimation of the reaction of the pupil to light is subject to a number of sources of error, which are due to the fact that the difference between the effect of light upon the macula lutea and upon the peripheral portions of the retina are disregarded, and also to the fact that the narrowing of the pupils by convergence and accommodation cannot be positively excluded. As a result of minute investigation, Schirmer[1] gives the following rules for the accurate study of the reaction of the pupils to light: "The patient should be seated at a distance of one meter from a well-lighted window which is not exposed to the direct rays of the sun. (See p. 1051.) After the eyes have adapted themselves to this illumination, the diameter of each pupil is observed; the reaction of each pupil to light is now determined by holding the hand in front of the open eyes and then rapidly withdrawing one of the hands. The reaction of each pupil to light is next determined while the opposite eye is unshielded from illumination." The reaction is more marked with the first method of examination (with the opposite eye shielded), since the exclusion of the crossed innervation causes the pupil to dilate before the reaction occurs, or, at least, to be more susceptible to light. This procedure is consequently the one best adapted for determining the vestiges of a diminished direct pupillary reaction. The crossed pupillary reaction is then determined by observing the eye, while the opposite one is alternately shielded and exposed. This investigation is repeated for each eye. The sum total of the direct and crossed pupillary reactions, and consequently the last remnants of a diminished reaction of the pupils to light, is best estimated by shielding both eyes, simultaneously exposing them, and then observing the reaction of both pupils.

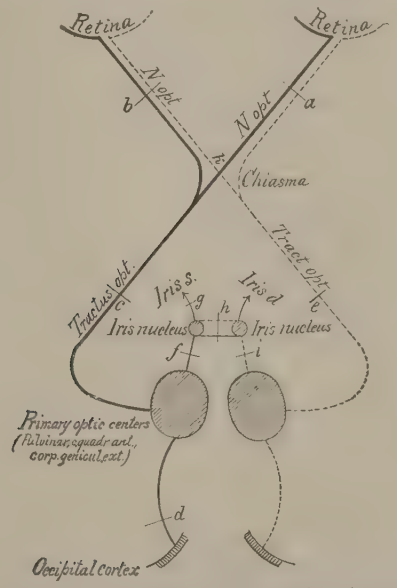


Fig. 412.—Old diagram of the pupillary light reflex, which no longer obtains. The primary optic centers (pulvinar, corpus geniculatum externum, and anterior corpora quadrigemina) are represented as a single center for the sake of simplicity. (See Fig. 400.)

See p. 1056 et seq. concerning the so-called "hemiopic reaction," *i. e.*, hemiopic rigidity of the pupil.

Fig. 412 represents the course of the light reflex which was formerly accepted as accurate. It was based upon the supposition that the stimulus to the iris nucleus, causing a reflex narrowing of the pupil, originated in the so-called primary optic centers (pulvinar, anterior cor-

[1] Deut. med. Woch., 1902.

pora quadrigemina, and corpus geniculatum externum, see Fig. 400). The bilateral character of the light reflex was attributed not only to the semidecussation of the optic fibers, but also to the bilateral connection of the iris nuclei. (See Fig. 412.)

Although the above conception was advocated in the earlier German editions of this work, it is no longer tenable, because it has been proved clinically, as well as experimentally, upon animals, that lesions of the primary centers do not cause any disturbances of the pupillary reflex. We must, therefore, conclude that the sensory fibers, which transmit the pupillary light reflex, are distinct from the visual fibers, and certainly leave the optic tract before its entrance into optic centers. Physiologic examinations and clinical observations induced Bechterew [1] to con-

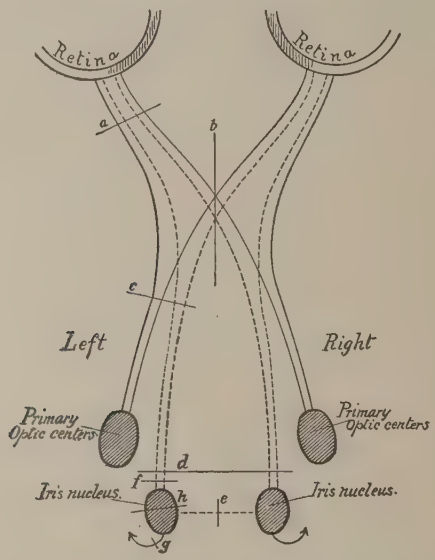


Fig. 413.—Diagram of the pupillary light reflex. The continuous lines represent the visual fibers; the dotted lines, the centripetal fibers for the pupillary light reflex. The central tract for contraction of the pupil by convergence and accommodation is not indicated in the figure; it might be imagined as passing to the iris nucleus from the side.

clude that special pupillary fibers exist in the optic nerves and that these fibers, after separating from the visual fibers at a certain distance behind the chiasm, run through the gray matter near the third ventricle to the iris nucleus.

Owing to the occurrence of hemiopic pupillary immobility, it must be assumed that the fibers of the optic nerve which transmit the pupillary reflex undergo a semidecussation in the chiasm in the same manner as do the visual fibers.

Bechterew's diagram for the pupillary light reflex, which was reproduced in the second German edition of this work, does not sufficiently explain physiologic conditions; it contained no fibers whatever for the

[1] Deut. Zeit. f. Nervenheilk., vol. xvi, parts 3 and 4, p. 193 et seq.

direct pupillary reaction, and certain of its details had not been positively confirmed. The author believes that the following diagram (Fig. 413) of the pupillary reaction will explain the physiologic and pathologic facts now at our disposal without necessitating any further unwarranted suppositions. The previously mentioned and more recent anatomic postulates have been considered in its construction.

The lesions most important from a clinical standpoint are indicated in the diagram by the letters *a, b, c, d, e, f, g,* and *h*. The clinical symptoms of these lesions are as follows:

Lesion *a:* Transverse section of one optic nerve. Blindness and absence of the direct pupillary reaction in the eye of the same side, with retention of the crossed pupillary reaction. The crossed reaction is absent in the opposite pupil.

Lesion *b:* Sagittal section of the chiasm. Bilateral temporal hemiopia. The direct and crossed pupillary reactions are normal in both eyes when tested in the usual manner by diffuse light. Direct and crossed hemiopic pupillary immobility in both eyes (p. 1056, Note 2) from involvement of the nasal halves of both retinas.

Lesion *c:* Section of one optic tract in front of the primary optic center and before the partial decussation of the centripetal fibers for the pupillary reflex. Homonymous hemiopia and homonymous hemiopic crossed and direct pupillary immobility (see below). Normal direct and crossed pupillary reaction by the ordinary test with diffuse light.

Lesion *d:* Involvement of all the centripetal fibers of the pupillary light reflex upon both sides after their separation from the visual fibers. Absence of the crossed and direct reactions of both pupils to light, with retention of visual power, normal movements of the eyeballs, and normal reaction of the pupils for convergence and accommodation (Argyll-Robertson's symptom in tabes dorsalis and progressive paralysis, p. 1058).

Lesion *e:* Injury to the fibers connecting the centers. The direct and crossed pupillary reactions normal in both eyes when tested with diffuse light. But only the direct reflex is present when the temporal halves of the retinas are tested, and only the crossed reflex is present when the light falls upon the nasal halves.

Lesion *f:* Section of the centripetal fibers for the pupillary light reflex proceeding from the left halves of both retinas. Homonymous hemiopic pupillary immobility in both eyes upon illumination of the left halves of both retinas. With diffuse illumination the direct and crossed pupillary reactions of both eyes are normal. The visual power and pupillary reaction for convergence and accommodation are maintained in both eyes. (See p. 1059.)

Lesion *g:* Section of the motor fibers leading from one iris nucleus to the pupil of the same side. Immobility of the affected pupil to light, both direct and crossed, and also during convergence and accommodation. The opposite pupil reacts normally both to direct and crossed impulses, and also to accommodation and convergence. The acuity of vision and the visual fields are normal in both eyes.

Lesion *h:* Destruction of the left iris nucleus. Immobility of the left pupil, both to direct and crossed-light impressions and also during accommodation and convergence. This is associated with hemiopic immobility of the right pupil during illumination of the left halves of the retinas.

A number of direct observations are still necessary to demonstrate the complete accuracy of the diagram. No observations of types *e* and *f*, for example, have as yet been published. In type *h* investigations have not been made to determine whether hemiopic immobility of the opposite pupil is really present from an involvement of the retinal halves corresponding to the injured side. Not until positive statistics have been obtained in reference to these points can this diagram be defended as absolutely correct. If it be found that the lesions *e*, *f*, and *h* do not materialize in actual practice, the diagram must be modified.

Hemiopic Pupillary Immobility (*Hemiopic Pupillary Reflex*).—Fig. 413 furnishes a key to the comprehension of the so-called hemiopic pupillary reaction (Wernicke) or hemiopic pupillary immobility. When one side of the optic tract is injured at the point *c*, or when the centripetal fibers of the light reflex proceeding from homonymous retinal halves are injured in the neighborhood of the point *j*, the result must be that the light reaction from the corresponding homonymous retinal halves of both eyes will be entirely abolished, whereas from the opposite retinal halves the reflex will remain normal. To this peculiar condition Wernicke gave the name *hemiopic pupillary reaction;* but von Leyden quite properly substituted for this expression the term *hemiopic pupillary immobility*, because, as a matter of fact, when this condition appears, what is observed is certainly an immobility or rigidity. In order to demonstrate this rigidity it is essential, while watching the pupillary condition, that each retinal half be lighted separately.

The ordinary procedure consists in projecting a cone of rays into the eye from one side by means of an ophthalmoscope or of a focusing lens, and by observing the reaction of the pupils, according as the light impinges upon the left or upon the right retinal half. A darkened room is, of course, very desirable, if not essential. The difficulty in this depends upon the uncertainty of confining the illumination to one of the retinal halves. If the actual apex of the cone of light does not impinge upon the retina, anterior or posterior circles—radiations—of the light picture may affect the other retinal half or even the macula, and so spoil the test. According to Salomonsohn,[1] the best result can be obtained by reflecting upon the patient's face, from a concave mirror, placed horizontally beside the eye, a very sharp and vertical flame picture (the latter is collected by the mirror from an illumination situated at one side). Then, by turning the mirror slightly, the reflected light passes the pupillary edge and impinges upon the retina, first from the temporal, then from the nasal, side. It is essential that the patient should always focus at the same distance, preferably into space. On account of the difficulties mentioned above (the dispersed circles of light), the results from this method are oftentimes not very conclusive; hence the following modification may be attempted: A black screen, at least a meter square and with a central opening, is placed vertically in front of the patient in the dark room, at a distance of about 60 cm. (about 2 feet). While the patient focuses upon the opening, an assistant in front of the screen projects a very bright illumination (kerosene or electric lamp) into the visual field, at one time from the right and another from the left side, but not near the focusing point of the patient, and then the behavior of the pupils is noted through the opening in the screen. The lamp should always be held at about the same distance from the eyes as a focusing point, in order to be sure that a sharp flame and not dispersed circles are projected upon the retina; with this method the test can be made as well with one eye as with two. If the pupils of both eyes contract only when illumination is at the right side, or only when it is at the left side, right or left hemiopic homonymous pupillary rigidity is present.[2]

The difficulty of both these tests consists in the fact that ordinarily a stimulation of the peripheral portions of the retina by a circumscribed light picture excites

[1] Deut. med. Woch., 1900, No. 42.

[2] In the more unusual temporal form of hemiopia which characterizes tumors in the neighborhood of the chiasm (acromegaly) and hydrocephalus (in which the chiasm is compressed by the enlarged infundibulum), we are compelled to examine for hemiopic pupillary rigidity in the corresponding inner retinal halves. (See Fig. 413, lesion *b*.) But, as a matter of fact, the demonstration of hemiopic rigidity has no local diagnostic significance in this form of hemiopia, as it can arise only in the chiasm.

only a weak pupillary reaction unless the region of the macula[1] is actually stimulated as well. This objection applies particularly when the sensitiveness of the entire retina has been somewhat impaired, *e. g.*, with a choked disk. In such cases the following device may be helpful. Place in front of the patient a screen which rotates upon a sagittal axis, and one half of which is white, the other half black; then instruct the patient to focus upon a small mark in the black half of the screen near the border between the black and white, and suddenly illuminate the screen very brilliantly by means of a light placed behind the patient's head. Now, if the patient alternately open and shut his eyes, hemiopic pupillary rigidity can be demonstrated by the pupillary reaction occurring only when the white side of the screen corresponds to the normal retinal half. This method may be employed for one as well as for both eyes in homonymous hemopia; in heteronymous (temporal) hemiopia, on the contrary, it can be used only for one eye.

In a case of acromegaly where even this device left the author in doubt, he employed the following method with considerable success. While the patient focuses upon some object (*e. g.*, his own fingers), at a distance of about 30 cm. (10 in.), an assistant projects in front of his eyes, at a distance of 30 cm., first from one side, then from the other, an electric bulb light of at least 32 candle-power, and stops just before the middle of the visual field; this light must be held so that the plane in which the carbon thread is bent remains parallel to the sagittal plane of the eye examined. With hemiopic rigidity the pupillary reaction can be obtained only from the retinal half whose pupillary fibers are preserved. The advantage of employing such an illumination is that by virtue of the linear character of the source of light, it remains sufficiently localized despite the presence of dispersed rays, to illuminate only one retinal half so long as the lamp does not approach too near the point focused. The great intensity of the illumination is an additional advantage.

Probably the best method of demonstrating hemiopic pupillary immobility known at present is performed by means of the "pupil tester," described by von Fragstein and Kempner,[2] which the author also has had an opportunity to employ. This is a small tubular instrument in which the rays from an incandescent lamp of 8 volts are condensed by lenses and diaphragms to a slender but most intense slightly convergent cone of light, the focus of which is situated 4 cm. in front of the anterior extremity of the instrument. With this cone of light it is easy to illuminate either half of the retina by projecting through the pupil from the temporal or the nasal side. Since the slightly convergent rays cross or become divergent 4 cm. in front of the instrument, an intense and quite circumscribed illumination of an individual portion of the retina is best assured by holding the instrument 3.3 cm. in front of the cornea, so that the focus of the cone of light falls about 7 mm. behind the convexity of the cornea. This situation corresponds to the nodal point of Listing's reduced eye, and rays passing into the eye and directed toward this point are peculiar in that they pursue their original direction through the vitreous humor as though they had not been refracted. With this position of the instrument the cone of light passes into the eye as though no refracting media were present, *i. e.*, the slightly convergent rays continue their original course into the interior of the eye as a slender, slightly divergent cone. This instrument is probably the only one with which it is possible to illuminate still more circumscribed retinal areas, such as a particular quadrant.[3]

The demonstration of hemiopic pupillary rigidity permits us to differentiate a so-called peripheral from a central homonymous hemiopia. While, according to Fig. 413, peripheral hemiopia (location of the lesion at *c*) produces hemiopic pupillary rigidity, this is not the case with central hemiopia (location of the lesion at *e*, above the primary optic centers, Fig. 400). The hemiopic pupillary rigidity in which total double blindness, composed of two hemiopias, one side of which is peripheral and the other central, occurs, is of special interest and has often been observed. An individual with these two lesions is completely blind. The accurate localization and significance of the visual disturbance then furnished by the presence of hemiopic immobility in the pupil which reacts only to one retinal half.

In those cases where hemiopic rigidity is present, both a direct and crossed

[1] Hess (Arch. f. Augenheilk., 1907, vol. lviii) showed that pupillomotor fibers exist only in the perimacular field, for a distance of about 3 mm., but not in the remainder of the retina. In a case of peripheral injury to one optic nerve Veraguth (Neurologisches Centralbl., 1908, No. 9) found that the pupillary reflex was lost though the eye retained a fairly large peripheral field of vision.

[2] Klin. Monats. f. Augenheilk., 1899.

[3] This instrument may be obtained from Reiniger, Geppert, and Schall.

pupillary reaction can be obtained by testing the pupils in the ordinary way, so that both retinal halves receive light. The reaction may be diminished, but it is still plain enough. In order to avoid overlooking hemiopic rigidity the tests mentioned above must be accurately made, especially in all cases of homonymous hemiopic and bilateral blindness following a cerebral affection. It is clear (Fig. 413, lesion *f*), however, that homonymous pupillary rigidity may occur without any visual disturbance.

Certain other purely hypothetic conditions of hemiopic pupillary immobility have been given in the tabulation of the various lesions of the pupillary reflex upon p. 1055 et seq.

The technical difficulties in determining homonymous pupillary rigidity described above are perhaps the reason that the phenomenon has been so rarely found.

An additional difficulty is furnished by disturbances of Haab's so-called cortical pupillary reflex, which is brought about by concentration of the attention upon a lateral source of light. (See p. 1059.) All the procedures for testing hemiopic pupillary immobility are of such a character that the attention of the patient is apt to be concentrated upon the light itself. But this is, of course, the case only when the light falls on the normal retinal half, and, therefore, if Haab's reflex be lacking, hemiopic pupil rigidity may apparently be present when the blind retinal half is lighted.

Loss of Pupillary Light Reaction (Pupil then Ordinarily Dilated); Rigidity of the Pupil to Light.—A failure of the pupil to react to light occurs in severe disturbances of consciousness of the most varying kinds; in cerebral pressure (in these cases bilateral); in poisoning from the substances mentioned above as dilating the pupils (these unilateral or bilateral, depending upon the poison); in focal lesions which interrupt the reflex pupillary arc on one or both sides in the manner detailed in Fig. 413 (*e. g., motor lesions*); in complete peripheral oculomotor paralysis; in nuclear oculomotor paralysis which affects the iris nucleus, but does not attack the other branches of the oculomotor (see p. 1045); in *sensory lesions;* in affections of the retina; and in bilateral optic atrophy or marked bilateral choked disk. Complete loss of pupillary reaction from choked disk is a comparatively exceptional occurrence, and observed only when the choked disk has caused blindness at the same time. The visual acuity is frequently very well preserved, and corresponds well with the slight injury to the conduction of the sensory fibers belonging to the pupillary reflex. Even when a lesion of the optic nerve diminishes the acuity of vision decidedly, the pupillary reaction need not be seriously impaired. This is evident without further explanation when we remember (p. 1054) that the centripetal fibers of the light reflex in the optic nerve are distinct from the visual fibers. A unilateral loss of reaction is usually associated with a dilatation of that pupil, as compared with the opposite side.

Ordinarily, complete examination of the condition of the optic nerve, on the one hand, and of the nerves supplying the eye muscles, on the other, facilitates a differential diagnosis between pupillary rigidity depending upon a lesion of the motor and that depending upon a lesion of the sensory segment of the reflex arc. Fig. 413 should always be consulted to comprehend the diagnostic points. In addition to other characteristics, it should be emphasized that with lesions of the motor segment of the pupillary reflex arc (in the nucleus of the iris or in the peripheral oculomotor), the narrowing of the pupil to accommodation and the power of convergence (see below under γ) is lost; whereas this is not the case when the loss of pupillary reaction depends upon a lesion of the retina or of the optic tract. In case the lesion is recognized as motor, the question is: Does this lie in the nucleus or its immediate neighborhood, or in the peripheral motor fibers of the oculomotor. This question is frequently decided by the behavior of the ciliary muscle, *i. e.*, by accommodation. In lesions of the nucleus or its neighborhood, accommodation may be preserved on account of the structure of the oculomotor nucleus (discussed upon p. 1045); whereas with a purely peripheral oculomotor paralysis, which may be situated in the trunk of the nerve or in the short branches of the ciliary ganglion, accommodation will probably fail.

Argyll-Robertson's Phenomenon (see p. 1055, *d*).—This is an early and important symptom of tabes dorsalis and of progressive paralysis. It consists in a preservation of the pupillary reaction to convergence and to accommodation, with a loss of the reaction of the pupil to light, and is not necessarily associated with any impairment of vision. (See p. 1059, γ.) For some unknown cause the pupils are generally narrowed (the so-called spinal miosis of tabetics).[1] Ordinarily the reaction of the pupils to pain is also wanting (see below under β). Erb called Argyll-Robertson's phenomenon a

[1] It has, however, not yet been proved that this is of spinal origin.

reflex pupillary rigidity, an expression in which the words, according to the author's opinion, are not used in their ordinary sense, since from it one might conceive of a rigidity occasioned reflexly, not of a rigidity of the reflex. The symptom has not yet been satisfactorily explained by anatomic researches. According to Bechterew, however, it must theoretically depend upon a lesion of all the centripetal fibers of the pupillary light reflex, either in the trunk of the optic nerve or after their separation from the visual fibers (lesion *d*, Fig. 413). It cannot depend upon a lesion of the motor segment (lesion *g* or *h*, Fig. 413), because the pupillary contraction in accommodation and convergence persists. F. Schultze noted the Argyll-Robertson pupil as a manifestation of toxemia in pneumonia. It is also frequently seen as a transitory phenomenon after epileptic attacks.

Paradoxic Pupillary Reaction.—This phenomenon, first described by Obersteiner and then by Bechterew, consists in the occurrence of a dilatation instead of a contraction of the pupils to direct and crossed illumination. At times a very insignificant initial contraction precedes the dilatation. Like the Argyll-Robertson phenomenon, this sign occurs principally in *tabes dorsalis* and *progressive paralysis*.

According to one conception, probably erroneous, this is a consensual or reflex dilatation depending upon unnoticed divergent movements of the eyeball at the moment of illumination (as contrasted with the narrowing of the pupils, associated with convergence and accommodation, see below, γ). Bechterew, however, considers that it is a phenomenon of fatigue, because, under the pathologic conditions mentioned above, a brilliant illumination fatigues, and so inhibits, the pupillary tonus after a scarcely noticeable or absent narrowing.

β. **Pupillary Pain Reflex.**—The stimulus of severe pains applied to various parts of the body, but more especially painful irritation of the skin of the neck, will usually dilate the pupils. This dilatation is produced by the pupillary dilator fibers of the sympathetic, derived from the eighth cervical and first dorsal segments. (See Fig. 462, p. 1149.) The reflex is sometimes useful in diagnosis, pointing to an involvement of of the roots or of the sympathetic. According to the author's experience, however, the pupillary pain reflex in man is so inconstant that, generally speaking, a difference between the two sides is the only sign worth heeding.

γ. **Narrowing of the Pupils to Convergence and to Accommodation.**—Physiologically, the pupils are decidedly contracted by efforts at convergence or accommodation (it is difficult to separate one from the other). The consensual movement is diagnostically significant: in the first place, because it shows that in testing the other pupillary reactions we must be careful to have the patient avoid convergence or accommodation. Perhaps the best plan is to have him always focus for the same distance, preferably into space. A further diagnostic interest is furnished by the retention of the convergence and the accommodation reflex, while the light reflex is absent, which proves that the light reflex is not affected by a lesion of the motor tract.

(See above: Loss of Pupillary Reaction to Light, p. 1058; Argyll-Robertson's Phenomenon, p. 1058.)

δ. **Westphal's Pupillary Phenomenon.**[1]—This consists of a contraction in the pupil when the examiner, by forcibly holding the lid open, prevents the patient's attempt to close the eye (Bell's phenomenon, p. 1075). To appreciate this reaction it is generally essential that the pupil in question should not react to light, or, at least, only slightly, and should not be markedly narrowed. It is most distinct when the pupils are dilated. Westphal never found the phenomenon in healthy individuals, and only once in the pupils of a hysteric person. He found it several times, on the contrary, in tabes and in progressive paralysis. The author has repeatedly observed it in tabes.

ε. **Haab's So-called Cortical Pupillary Reflex.**—Thus far no diagnostic significance has been attached to this reflex, though perhaps it may yet be utilized in the diagnosis of cortical disturbances of vision. It consists of a narrowing of the pupils when the patient, in a dark room, without any alteration in the position of the eye, concentrates his attention upon a flame placed at one side, *i. e.*, seen indirectly.

9. Behavior of the Accommodation

Before testing the accommodation, the acuity of vision must first be determined and any error of refraction corrected. To correct the latter, if the patient be myopic, we employ the weakest concave lens

[1] Neurologisches Centralbl., 1899, No. 4.

with which he sees distant objects most clearly; if hypermetropic, the strongest convex lens. The acuity of vision is then determined in the ordinary way. The accommodation is then tested by placing before the eye under examination, at a distance of 25 cm. in a good light, the finest test-type which he should be able to read at this distance with his acuity of vision. (Perfect accommodative power presupposed.) If he can read this type, the accommodation is, at least, normal. If he cannot, his accommodation must be defective. Such a defect will consist of the physiologic presbyopia of his age, plus whatever accommodative paresis may exist. The convex lens which the patient requires for reading the selected type at 25 cm. distance (plus the glass which corrects the refraction) measures the defect of accommodation in diopters. By comparing this defect with that which is found in a patient as a result of the physiologic presbyopia for his age (see the accompanying table), we can decide whether there is a paresis or paralysis of accommodation. Should the patient need a + 4 D. lens to read the type clearly, there exists no power of accommodation.[1] Such a total defect is physiologic after the age of seventy-five years (see table); but in younger individuals it would indicate a complete pathologic paralysis of accommodation. If a patient forty-five years old require a glass of + 2 D. he has, in addition to his physiologic presbyopia (0.5 D., according to the table), a paralysis of accommodation of 1.5 D., etc.

Age.	Degree of presbyopia, *i. e.*, the physiologic defect of accommodation in diopters.
Forty-five years	0.50 D.
Fifty "	1.50 D.
Fifty-five "	2.25 D.
Sixty "	3.00 D.
Sixty-five "	3.25 D.
Seventy "	3.75 D.
Seventy-five "	3.75 D.

We find a paralysis of accommodation in total oculomotor paralysis, in lesions of the *accommodation nucleus* (p. 1045), in *diphtheric paralysis*, and also after administration of atropin. Despite the fact that many diphtheric paralyses are probably peripheral in their localization, they are quite apt to involve the fibers of the oculomotor nerve which supply the ciliary muscle, whereas the pupillary fibers usually escape.

FIFTH CRANIAL NERVE; TRIGEMINUS

1. **Motor Trigeminus.**—The motor branch of the trigeminus supplies the muscles of mastication. Their power is tested by having the patient bite upon some object, such as a piece of cork or wood, or by having him exert vigorous movements of the jaw while the examiner attempts to hold the jaw still.

Unilateral weakness of the masseters may be recognized by placing, first on one side and then on the other, a flat piece of wood or spatula between the molars, and determining how firmly the patient can hold

[1] For the total optical effort required equals that which is necessary to focus upon the retina rays which come from a distance of 25 cm., in an eye rendered emmetropic by the correction of its refraction. This takes place when the convex lens in question renders parallel the rays which enter the eye from that distance. A lens of + 1 D. renders parallel rays which come from a distance of 1 m.; a lens of + 4 D. renders parallel rays which come from one-fourth of that distance, viz., 25 cm.

it by the action of these muscles. Palpation of the muscle itself during contraction also gives a good idea of its functionating power. The masseter also gives a good idea of its functionating power. The masseter muscle is best felt on the anterior border of the ascending ramus of the mandible, either through the cheeks or from the inside of the mouth. From the inside of the mouth we may also feel the contraction of the internal pterygoid, which lies opposite to the masseter and is separated from it by the mandible. The buccinator muscle is innervated by the trigeminus as well as the facial nerve. Its contraction can be felt by placing the finger in the mouth and directing the patient to press it actively against the alveolar process of the maxillary bone with his cheek. The mylohyoid and the anterior belly of the digastric are likewise innervated by the trigeminus, but this contraction is difficult to demonstrate. If, however, the patient with his mouth closed press his tongue against the hard palate, the floor of the mouth from the outside feels softer on the paralyzed side.

In regard to the action of the individual chewing muscles, we must remember that adduction of the lower jaw, *i. e.*, the closure of the teeth, is accomplished essentially by the temporal and masseter muscles. The external pterygoid pushes the lower jaw obliquely forward out of the glenoid fossa upon the articular tubercle (Gegenbauer). The bilateral action of the two external pterygoids protrudes the lower in front of the upper teeth. The unilateral action of one external pterygoid pushes the jaw to the opposite side, and the alternate action of the two external pterygoids—presupposing, of course, that the temporal muscle pulls the lower jaw back again into the glenoid fossa—causes the movement of mastication. The external pterygoid also aids in opening the mouth, and this is further assisted by the force of gravity, and by the digastric [1] and the platysma myoides muscles.[2] The internal pterygoid muscle aids the temporal and the masseter in adducting the lower jaw, and also contributes, to a certain extent, in the movement of the jaw forward.

Cerebral *paralyses of the chewing muscles* are analogous to cerebral paralyses of the eye muscles. (See p. 1039.) They are always to be attributed to a cause lying in the neighborhood of the trigeminus nucleus or affecting the efferent trigeminus fibers. This depends upon the fact that above the nucleus the central fibers of each trigeminus are distributed to both hemispheres, in consequence of which a unilateral hemispheric lesion does not necessitate a crossed motor trigeminal paralysis, as the function of the intact hemisphere is sufficient to maintain the innervation of both sides. To comprehend this bilateral innervation, the reader should consult Fig. 403, for that diagram applies to the muscles of mastication in the same way as to the eye muscles. On the other hand, a bilateral paralysis of the chewing muscles can be brought about by bilateral hemispheric lesions, such as pseudobulbar paralyses (p. 1090). In hemiplegia a bilateral defect of innervation of the chewing muscles may perhaps be demonstrated with the dynamometer.

Spasm of the chewing muscles occurs as an accompaniment of general spasms, *e .g.*, the tonic spasms in tetanus and in meningitis, and reflexly from painful affections of the jaw, producing so-called lockjaw.

The so-called *jaw reflex* depends upon both the motor and the sensory trigeminus. It consists in a contraction of the chewing muscles which lifts the lower jaw, and is produced by striking the lower jaw, either directly with a percussion

[1] The anterior belly is innervated by the third branch of the trigeminus; the posterior belly, by the facial. [2] Innervated by the facial.

hammer or indirectly through some object applied to the jaw. It can be elicited in most healthy individuals, but is not absolutely constant. If the reflex be increased, a clonus can frequently be elicited by simply drawing the jaw downward (jaw-clonus, masseter-clonus).

The Palate Function of the Trigeminus.—The trigeminus takes part in the innervation of the soft palate, and supplies in great part the posterior arch, according to observations of paralysis of the trigeminus.[1] In unilateral paralysis of the motor root of the trigeminus the posterior arch of the palate hangs lower than that of the normal side, the uvula is twisted anteriorly and toward the paralyzed side. The latter phenomenon is not easy to explain, but it seems to be due to the fact that the side of the uvula corresponding to the posterior arch of the palate which hangs down is shortened and made tense, becoming concave on that side in a manner similar to the spring of an aneroid barometer. The bending forward is probably due to the fact that the dropping of the posterior palatine arch lessens the space at the posterior aspect of the uvula.

Auditory disturbances (diminution of hearing and subjective tinnitus) in cases of trigeminal paralysis have been referred to a paralysis of the tensor tympani. These symptoms are, however, inconstant and capable of many interpretations.

2. **Sensory Trigeminus.**—The sensory division of the trigeminus supplies the skin of the face, the mucous membranes of the mouth and nasal cavities, the conjunctiva, and the cornea. It also takes part in the function of taste (chorda tympani), and the function of smell in the nasal mucous membranes. The sensibility of the skin (touch, pressure, pain, and temperature) is tested just as was described above (p. 967 et seq.). In testing the trigeminus taste function, a soft brush moistened first with acid (weak acetic acid) and afterward with salt solution is touched to the tongue, and the patient asked to describe what sense of taste he experiences. The two sides of the tongue are compared, and it is readily determined whether the appreciation of taste is equally active and prompt upon the two sides. Since the trigeminus practically supplies only the anterior part of the tongue, the test should be made there, so as to exclude, so far as possible, the taste-fibers of the glossopharyngeal. The patient should keep his tongue protruded, and reply to the examiner's questions by nodding and shaking his head. It is, of course, advisable to include at the same time the examination of the sense of taste of the part supplied by the glossopharyngeal, employing the same method as above, but selecting the posterior part of the tongue. The patient should not breathe during the test, so as to avoid a confusion between the sense of smell and that of taste. The taste-fibers of the trigeminus (chorda tympani) may be injured in lesions of the lingual muscle (which they supply), in affections of the middle ear (through which they pass), in certain peripheral paralyses of the facial (see pp. 1070 and 1071), and finally in lesions of the root of the second or, according to other authorities, of the third branch of the trigeminus, in which the taste-fibers are diverted from the facial. (See Fig. 422.) Testing the sense of smell supplied by the trigeminus has been described already under the olfactory nerve. (See p. 1033.)

The *corneal sensibility* is determined by touching the cornea with the head of a pin. Normally, this procedure is rather painful, owing to the fact that, according to von Frey's researches, the cornea possesses no tactile points, but probably countless pain points. (See p. 968 et seq.) At the same time we should determine the preservation or absence of the so-called "corneal reflex" (lid closure in touching the cornea). The loss of this may depend upon a lesion of the sensory segment (tri-

[1] C. W. Müller and F. Schultze.

geminus), or of the motor segment (facial) of the reflex arc. Further examination will determine which.

Pareses of the sensory trigeminus occur in peripheral lesions of the nerve, in lesions of the trigeminus fibers emerging from the pons, and also accompany the hemianesthesias observed both in hysteria and in focal lesions at the most posterior part of the internal capsule. (See p. 1090 et seq.) Disturbances of sensibility which appear in the region supplied by the trigeminus from spinal cord affections involving the ascending (spinal) trigeminus roots are worth noting, because of their diagnostic importance. They may occur as low as the second cervical segment (syringomyelia).

(See Fig. 449, p. 1136, in regard to the distribution of the peripheral skin branches of the trigeminus.)

The peculiar so-called trophic disturbances of the conjunctiva, the mucous membrane of the mouth, and the cornea, caused by lesions of the sensory part of the trigeminus, are of interest, although the significance of the phenomenon has not yet been determined. Some assume that it is merely a diminution of the self protection of the tissue, because of the lost sensibility and the destruction of certain vasomotor reflexes. Others believe it to be due to the direct trophic influence of the sensory fibers of the trigeminus. Whichever explanation be correct, there is no doubt that so-called trophic disturbances occur and are directly connected with sensory trigeminus paralysis. The author once saw an exquisite neuroparalytic keratitis in a case of brain tumor, with almost complete paralysis of the sensory trigeminus. In this case, and also in a case of tabes with trigeminus anesthesia, peculiar ulcers developed at the corner of the mouth and on the buccal mucosa, which at first glance had the appearance of syphilitic or carcinomatous lesions. They were distinguished, however, by their very slight infiltration and a tendency to cicatricial contraction and healing. In the case of brain tumor, a trophic disturbance appeared on the outer surface of the cheek in the form of vesicles, caused by the moderate heat used in the test for thermal sensibility, while the normal side remained uninjured. In this case the trophic disturbances could not be explained by a disturbance of the vasomotor reflex, because gentle mechanical irritation of the skin produced a hyperemia similar to that of the healthy side. The objection to the assumption that sensory fibers can conduct direct centrifugal trophic impulses can no longer hold, because studies in the negative variations of currents have furnished direct experimental physiologic proof that motor and sensory fibers can conduct impulses in both directions, *i. e.*, sensory fibers can conduct centrifugally.

SEVENTH CRANIAL NERVE; FACIAL

The facial nerve, probably purely motor, supplies the facial muscles, including the muscle which closes the eye (orbicularis oculi), Horner's muscle, the platysma myoides, the muscles of the scalp (occipitalis and frontalis), the retrahens, attolens, and transversus auriculæ,[1] the stylohyoid, the posterior belly of the digastric, the buccinator, and finally, by means of the descending palatine nerves, which pass through the sphenopalatine ganglion of the second branch of the trigeminus it supplies, together with the glossopharyngeus, vagus, and spinal accessory, the muscles of the soft palate. The facial supplies the greater part of the latter. The palatoglossal and palatopharyngeal muscles (palatine arch and the azygos uvulæ) seem to be supplied mostly by the facial. In the Fallopian canal the facial nerve supplies the stapedius muscle by means of the stapedius nerves. At one part of its course in the temporal bone the chorda tympani is united to the facial nerve, contributing the taste-fibers to the facial, and receiving from it the salivary secretory fibers for the submaxillary and sublingual glands. (See p. 1070.) From its motor nucleus the facial receives fibers for sweat secretion, and, according to Goldzieher, the secretory fibers for the lacrimal glands. These, Köster[2] thinks, probably originate from the nuclear region of the glossopharyngeal. (See p. 1071.) At the periphery the facial oftentimes receives sensory fibers of the trigeminus.

[1] According to Heitzmann, the attrahens auriculæ is supplied by the auriculo-temporal branch of the third branch of the trigeminus.

[2] Arch. f. klin. Med., vol. lxviii.

(*a*) Paralyses of the Facial

General Symptomatology of Facial Paralyses.—Upon the paralyzed side in facial paralysis we notice an obliteration of the wrinkles, a loss or very slight preservation of the ordinary voluntary movements, and, under some circumstances, even the loss of the emotional movements, the associated movements, and the reflexes. If the paralysis be sufficiently marked, the affected cheek flaps with respiration like a boat's sail, especially during sleep, and if the branches to the eye be affected, the eye remains more or less open, despite attempts to close it and even during sleep (*lagophthalmus*). In early cases the mouth is drawn to the healthy side. If the palate also be paralyzed, it frequently hangs noticeably lower upon the diseased side and seems drawn to the healthy side, and voluntary or reflex movement draws it still more toward the latter. An oblique position of the uvula so often occurs normally that it is of no importance for the diagnosis of palate paralysis. (See p. 1062 in regard to the oblique position of the uvula and the behavior of the palate in motor paralysis of the trigeminus.) A unilateral palate paralysis will produce neither a nasal character in the voice nor regurgitation through the nose; but both phenomena will be observed if the palate be bilaterally paralyzed (diphtheric paralyses). If the eye be prevented from closing by an accompanying movement of the ocular branch of the facial, the normal flow of tears will be affected by paralysis of Horner's tear-sac muscle and a drooping of the lower eyelid. The patient will then suffer from a trickling of tears (epiphora), and very often eczema of the eyelid results. He may also complain of slight disturbances of vision on account of the corneal suffusion. *Blepharoplegia (loss of automatic winking) is marked even in complete facial paralysis (including the orbicularis oculi). This signifies that winking depends not merely upon facial innervation, but also upon relaxation of the levator palpebræ superioris.* In consequence of the disturbances of the flow of tears the nasal mucous membranes become drier than normal, and the sense of smell is, therefore, often affected. The nasal opening of the diseased side often seems narrowed from paralysis of the levator alæ nasi. Because of the paralysis of the muscles about the lips, the saliva frequently trickles from the corner of the mouth upon the paralyzed side and patients are unable to whistle. With pronounced facial paralysis the speech may be altered, especially the ability to articulate the labial letters. Statements vary considerably in regard to the condition of the tongue in facial paralyses. Probably facial paralysis as such has no influence upon the position of the tongue, although, since the facial nerve innervates the stylohyoid and the posterior belly of the digastric muscle, its paralysis may have a certain influence upon the position of the hyoid bone. In central facial paralysis the tongue deviates toward the paralyzed side, because here the hypoglossal nucleus, situated so near by, is always more or less affected as well. The deflection of the tongue in central facial paralysis is, therefore, the result of a paresis of the genioglossus muscle, which is supplied by the hypoglossal nerve. (See Twelfth Cranial Nerve, p. 1086.) Deflections of the tongue occur in peripheral paralysis, but these have only an indirect connection with the facial nerve, and their explanation is not the same in every case. For instance, in peripheral paralysis one would think at first glance that the tongue was protruded obliquely, but more

careful observation shows that it is really protruded in the middle line, the appearance of deviation being due to the twisted mouth. In other cases the tongue is actually deflected to the healthy side, which is exactly opposite to the condition in central facial paralysis accompanying genioglossus paralysis. Hitzig has proved that this depends upon the patient's effort to protrude his tongue obliquely in order to keep it in the middle of the twisted mouth. This can be confirmed easily by correcting manually the asymmetry of the mouth. The patient then protrudes the tongue exactly in the middle. Paralysis of the platysma myoides is most readily recognized by having the patient attempt to draw the lower lip downward as far as possible. Normally, the platysma assists in this movement, and the contracted fibers stand out quite

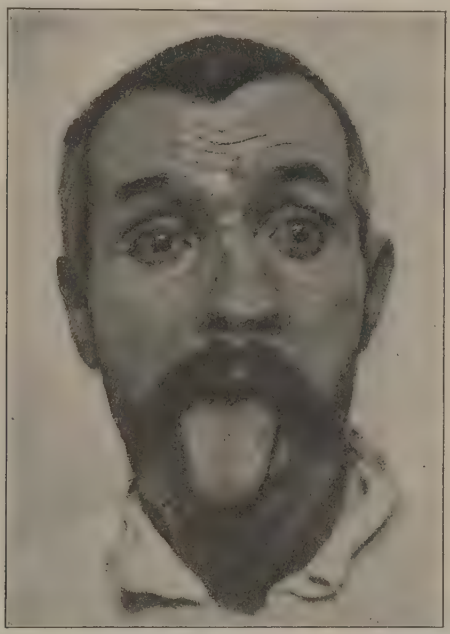


Fig. 414.—Facial asymmetry simulating hemiplegia. The distorted nose and a groove in the lower front teeth are responsible for the apparent deviation of patient's tongue to the right (New York City Hospital).

plainly under the skin of the neck, so that the contrast between the healthy and paralyzed sides can be readily recognized. A paralysis of the muscles of the ear (retrahens, attollens, and transversus auriculæ) and of the frontalis and occipitalis muscles can be readily recognized, but only in those patients who can move the ears and the scalp voluntarily. Yet, sometimes a paralysis of the ear muscles of one side causes a noticeable drooping of the ear.

The clinical picture of facial paralysis varies, moreover, according to the position of the paralysis, whether above the nucleus (*i. e.*, in the central neuron) or in or below the nucleus (*i. e.*, in the peripheral neuron). It becomes necessary, therefore, in the following discussion, to differentiate accurately the symptomatology of these two types of facial

paralysis, and to defer the discussion of the affections of secretion and taste as well as certain accompanying troubles with the hearing, until the peripheral type (the one which they accompany) is taken up.

Central (Supranuclear) Facial Paralysis.[1]—As is well known, the cortical center of the facial nerve lies at the foot (*i. e.*, the lowermost part) of the central convolution (see Figs. 424, 425, and 426, p. 1095), and from this point its fibers pass intermingled with the other pyramidal fibers through the internal capsule to the facial nucleus of the opposite side. In its course it is quite frequently injured (cerebral hemiplegia). Any lesion situated above the nucleus causes what we designate as central facial paralysis, involving the muscles of expression of the lower half of the face and the corresponding half of the palate upon

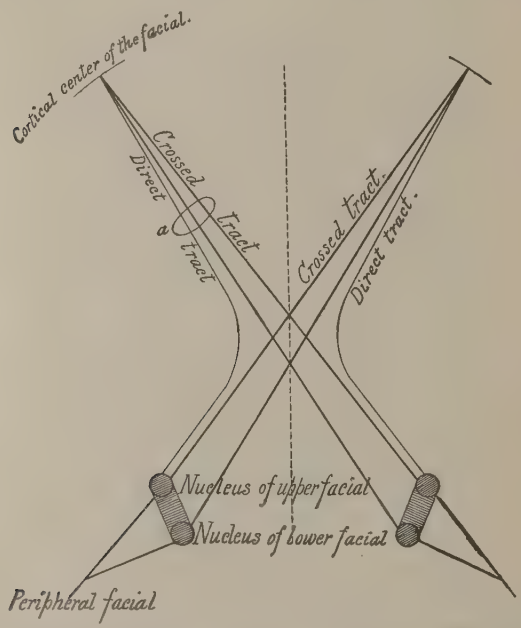


Fig. 415.—Diagram of the central innervation of the facial nerve. The upper branch is supplied from both hemispheres, more from that of the opposite side. The lower branch is supplied almost exclusively from the opposite hemisphere.

the affected side, whereas the secretory and taste functions of the facial are not affected at all, because the fibers supplying them do not join the facial nerve until it reaches the periphery. (See Nucleoperipheral Facial Paralysis.) Nor does this paralysis include the upper branch of the facial, which supplies the muscles for closing the eyes and the forehead muscles, for reasons about to be mentioned. In regard to the behavior of the tongue, see above, p. 1064.

The most weighty factor in differentiating between a central and a

[1] "Central" and "cerebral" should not be confused. A subnuclear or peripheral facial paralysis may be located within the brain, *i. e.*, still be cerebral, although it is below the nucleus, and therefore not central, but peripheral.

peripheral paralysis is the non-involvement of the upper facial branch (for the forehead and eyes) in the former. This peculiarity is to be explained by the supposition that only the lower part of the facial (the branch to the face) possesses an actual crossed innervation from the cerebral cortex, whereas the upper branch, like the eye muscles (see p. 1043) and the motor trigeminus, is equally innervated or nearly so by both hemispheres, so that any defect of innervation from one hemisphere is concealed or compensated for by the activity of the other.

A diagram of the central facial innervation, made in accordance with this supposition, is given in Fig. 415. This clearly explains how a unilateral cerebral lesion at (*a*) paralyzes only the lower, not the upper, facial of the opposite side, since the latter is still sufficiently innervated by the uncrossed tract.

The hypothesis responsible for Fig. 415, viz., that the facial possesses a separate nucleus for its lower and another for its upper branch, is really not based upon anatomic proof. But experience shows that a bulbar paralysis, a disease of the nuclei of the oblongata, affects almost exclusively the lower facial, which makes it probable that the nucleus of the latter exists functionally isolated, even though it is impossible to demonstrate this macroscopically. We have attempted to express this individuality as simply as possible in Fig. 415, by representing the two facial nuclei as connected.

It is, moreover, incorrect to assume that in a central paralysis the upper facial escapes entirely, for a more minute examination shows that a slight weakness can ordinarily be demonstrated. This consists in a less vigorous closure of the eye upon the affected side, and in the patient's inability to close the eye of the paralyzed side alone, although before the injury this was possible (*signe de l'orbiculaire,* Revilliod). From this it is evident that both hemispheres influence the upper facial, but that the effect of the crossed fibers outweighs that of uncrossed, although perhaps only to a slight extent. Fig. 415 suggests this by the heavier line representing the crossed fibers of the upper facial.

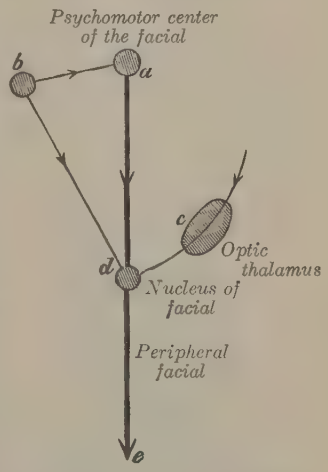


Fig. 416.—Diagram of the three functionally different central paths of the facial nerve and of its reflex arc.

Probably the central innervation of the stapedius muscle, which plays a rôle in the symptomatology of peripheral facial paralysis, behaves in the same way as that of the upper facial, so that in consequence of the bilateral innervation of the stapedius the symptom of hyperacusis (p. 1070) cannot be attributed to central facial paralysis.

In addition to the escape of the upper facial innervation, a central facial paralysis is further differentiated from a peripheral paralysis by the way in which certain voluntary movements and the emotional movements take part in the paralysis. To explain this point we must assume that tracts which are separated at least for a part of their course are responsible for each different kind of movement. Fig. 416 will serve as an illustration.

a Represents the psychomotor center of the facial; *b* represents another psychomotor center (*e. g.*, the arm-center); *c*, the optic thalamus; *d*, the facial nucleus.

The tract (*a d e*) represents the voluntary facial tract.

It has been assumed oftentimes that associated movements (*e. g.*, grimaces accompanying movements of an arm) depend upon hypothetic tracts like *b d*. To prove their existence it has been argued

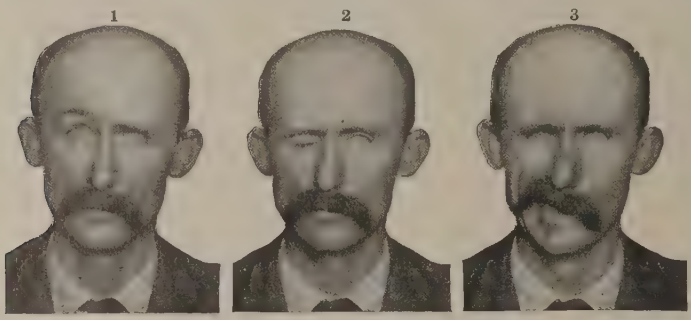


Fig. 417.—Facial palsy of left side: 1, Attempt to raise both eyebrows; 2, attempt to close both eyes; 3, smiling (Church).

that a slight central facial paralysis is sometimes evidenced only by a weakness of the associated movements, as compared with those of the healthy side, thus assuming the injury of a tract (*b d*), while the actual facial tract (*a d*) is unaffected. But this manifestation of a weakness of the associated movements in the facial territory in certain cerebral facial paralyses can also be explained in another way. The associated move-

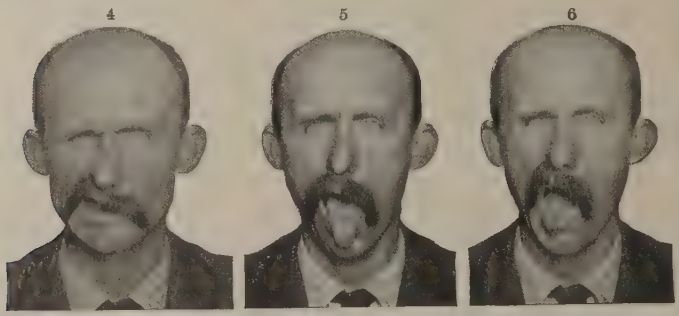


Fig. 418.—Facial palsy of left side: 4, Forced effort to uncover teeth on both sides; 5, protruded tongue in middle line; 6, mouth open more widely on sound side in bilateral effort (Church).

ments can be assumed to pass along the tract (*b a d*). Then a slight lesion of the voluntary tract, *a d*, offers no appreciable opposition to the voluntary impulse, but does to the weaker associated impulse running over *b a d*. The fact that a similar effect has been noted in mild cases of peripheral paralysis argues for this explanation (p. 1069, note 1). Hence it seems to the author superfluous to assume the existence of tracts like *b d* in order to explain associated movements.

The facial innervation of mimicry is probably from the tract *c d*, through the optic thalamus. This is determined from experience in affections of the optic thalamus or of its neighborhood, which cause isolated paralysis of the facial mimetic movements. Moreover, if the thalamus region be intact, ordinarily no, or only a very slight, involvement of the mimetic movements occurs in facial paralysis.

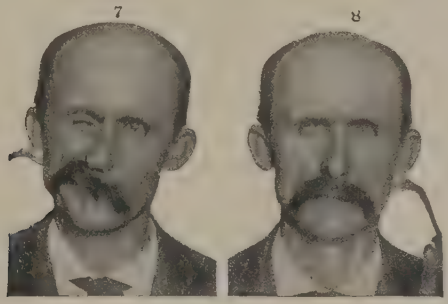


Fig. 419.—Facial palsy of left side: 7, Effect of faradism on sound side; 8, non-effect of same current on paralytic side (Church).

Besides the relative freedom from involvement of the upper branch, a central facial paralysis is characterized by intact reflexes and by the fact that the actual voluntary movements and the spontaneous movements need not be affected to the same degree, whereas without question, in lesions of the peripheral neurons situated somewhere along the line

Fig. 420.—Same case six months later. 9, Shows late contracture on the paretic side while the face is at rest; 10, contracture in the lower half of the face increased by gently closing the eyes, and at the same time shows weakness about left eye; 11, contracture increased by raising brows, showing overaction of zygomatici and weakness of frontalis on left side (Church).

d e (*i. e.*, in nucleoperipheral paralysis), both functions appear to be equally affected.[1]

In order to differentiate a central from a nucleoperipheral facial

[1] This is true, however, only for very decided and complete nucleoperipheral facial paralyses. In incomplete peripheral paresis, one frequently observes merely that the facial behaves differently for different kinds of movements, *e. g.*, that the paralysis is recognized only in laughing or in associated movements. Perhaps this can be explained by supposing that in the different kinds of movements (voluntary, spontaneous, associated, and reflex movements) the impulses vary in strength.

paralysis, it is obviously necessary to distinguish separately the different kinds of facial movements, to carry out the electric examination in accordance with the rules mentioned upon p. 1009 et seq., and to determine the presence or absence of degenerative atrophy of the paralyzed muscles in accordance with p. 1000 et seq. Of course, neither atrophy of the facial muscles nor electric changes occur in central facial paralysis.

Nucleoperipheral Facial Paralysis.—The general symptomatology of facial paralysis mentioned above (p. 1064 et seq.) must be amplified in the case of nucleoperipheral paralysis by the description of certain other disturbances of function peculiar to this type.

As most important may be mentioned the paralysis of the stapedius muscle. The motor fibers for the supply of this muscle leave the facial nerve within the petrous bone in order to reach the tympanic cavity. (See Fig. 421, p. 1072.) Although they probably also accompany the facial in its intracranial course, a stapedius paralysis is actually observed only in the peripheral form of facial paralysis, probably because the stapedius muscle, like the forehead and eye branches of the facial, is innervated by both cerebral hemispheres. (See p. 1067.) This paralysis of the stapedius, observed in certain localizations of peripheral facial palsy, of which we shall speak later more fully, is sometimes manifested by a characteristic peculiarity of hearing, designated as hyperacusis. In this condition the patient hears the deep tones (and sometimes others) louder upon the paralyzed side, and oftentimes in a very annoying fashion; sometimes the sound impression is combined with a sensation of pain. Lucae has attributed this phenomenon to an increased tension of the tympanic membrane, producing a rise of pressure in the labyrinth, because the action of the tensor tympani (innervated by the trigeminus) can be no longer counteracted by its antagonist, the stapedius. This explanation coincides with the modern conception, which assumes that the tympanic membrane, together with the chain of ossicles and their muscular apparatus, serves much less for sound transmission than for a so-called accommodation of the acoustic organ to the different kinds of sound impressions, and for the protection of the internal ear against too intense sounds, associated with marked pressure variations in the labyrinthine fluid. Patients with paralysis of the stapedius muscle also occasionally complain of experiencing subjective noises in the ear from movements of the facial or chewing muscles.

Other peculiar phenomena occur in peripheral facial paralysis when the fibers of the *chorda tympani* are injured. These consist partly of disturbances in the senses of touch, of pain, and of taste upon the anterior half of the tongue, partly of disturbances in the salivary secretion of the submaxillary and sublingual glands. Patients frequently complain of a defective sense of taste upon one side of the tongue, or of an abnormal dryness of the corresponding half of the mouth. (See p. 1062 et seq. for the more exact method of testing the sense of taste.) To examine the chorda tympani's function of salivary secretion more accurately the following procedure is advisable: The patient opens his mouth and lifts the tip of his tongue so as to expose the openings of the ducts of the submaxillary and sublingual glands (ordinarily united at the sublingual caruncle). In case he is unable to do this, the tip of the tongue is held up by a pair of tongue forceps. The sublingual caruncle is then carefully dried upon both sides of the frenum with absorbent cotton, and while the examiner watches carefully the openings of the

ducts, the patient inhales deeply the fumes from a sponge saturated with acetic acid, and held close to the nose. If the chorda functionate normally, the saliva flows from both sides freely, as a result of the reflex; if the chorda be paralyzed upon one side, the flow occurs only upon the healthy side or much more profusely upon that than upon the injured side.

The excretory ducts are occasionally so close together that the above method will not enable us to determine whether saliva comes from one or both openings. In these cases the author has succeeded in gently clamping the excretory duct upon the unaffected side with a cilia forceps, after which it is easy to observe whether saliva escapes from the opposite opening.

In connection with the anatomic relations of these two functions of the chorda to the facial, we should emphasize the fact that the function of secreting saliva belongs to the facial from its origin at the base of the brain up to the exit of the chorda tympani. According to Köster,[1] it probably does not arise from the facial nucleus itself, but from the nuclear region of the portio intermedia Wrisbergi belonging to the glossopharyngeal. The taste-fibers of the chorda tympani, on the contrary, accompany the facial from the periphery through the tympanic cavity, merely a tiny distance apart, and leave the latter again near the geniculate ganglion in the petrous bone (Fig. 422), according to one supposition (continuous blue line), in order to connect with the sphenopalatine ganglion by means of the large superficial petrosal nerve, and from there with the second branch of the trigeminus, but according to another less probable view (dotted blue line) in order to connect with the third branch of the trigeminus or with the glossopharyngeal by means of the communicating nerve to the tympanic plexus.

Our knowledge of the functions of the peripheral facial has been still further perfected by Goldzieher. He found that at the base of the brain the trunk of this nerve contains fibers for the secretion of tears, and that, therefore, an injury to the facial at this point results in drying up the tear secretions[2] upon the paralyzed side. These secretory fibers must emerge from the facial further down in the region of the geniculate ganglion and pass by means of the greater superficial petrosal nerve to the sphenopalatine ganglion, and from there to the lacrimal glands, by means of the communication between the subcutaneous malar and the lacrimal nerves. Goldzieher's suppositions have been confirmed by an observation of Franke,[3] as well as by the extensive clinical and experimental work of Köster.[4] According to the latter, the lacrimal secretory fibers, like the salivary secretory fibers, probably arise from that part of the glossopharyngeal nucleus belonging to the portio intermedia Wrisbergi, and mingle with the facial directly at its exit from the brain. To test the lacrimal secretion, he recommends tickling the nasal mucous membrane with a feather or with a fine brush, and then observing the secretion. The amount of the tear-flow secreted can be best estimated by collecting it upon a piece of filter-paper introduced into the conjunctival sac.

Köster, in addition, showed that disturbances of the sweat secretion

[1] Deut. Arch. f. klin. Med., 1900, vol. lxviii.

[2] That is, there is only intermittent secretion from the tear-glands, such as occurs in weeping or in reflex tears, not a continued conjunctival secretion.

[3] Deut. med. Woch., 1895, p. 33.

[4] Loc. cit.

upon the paralyzed half of the face appear not uncommonly in peripheral facial paralysis. This, too, is to be attributed to the fact that from its nucleus the facial conducts fibers for the secretion of sweat. In peripheral facial paralysis these fibers may be stimulated (hyperhidrosis) as well as paralyzed (anhidrosis). These phenomena may be confused with the influence of the sympathetic upon the sweat secretion of the face.

Slight disturbances of hearing readily occur in lesions of the facial nerve in the neighborhood of the geniculate ganglion. These depend

Fig. 421.—Diagram of the peripheral nerve-fibers of the facial for clinical use.

upon the proximity of the internal ear to the facial nerve at this point (the cochlea is separated by a layer of bone about $\frac{1}{4}$ mm. thick). Hence inflammatory changes of the facial can easily affect the internal ear.

The distinctions between nucleoperipheral (*i. e.*, facial paralysis in the region of the peripheral neurons) and central facial paralysis have already been emphasized in describing the latter (p. 1066 et seq.). From this it is evident that the essential factors in the distinction are the definite paralysis of the forehead and eye branch of the facial in the nucleoperipheral forms, disturbances in the secretory and taste functions,

the condition of the tongue (p. 1064), the condition of the reflex and spontaneous movements (p. 1068), and the electric and trophic conditions of the muscles. After the nucleoperipheral nature of a facial paralysis has once been recognized, the chief interest centers in determining the exact location of the lesion in the course of the nucleoperipheral

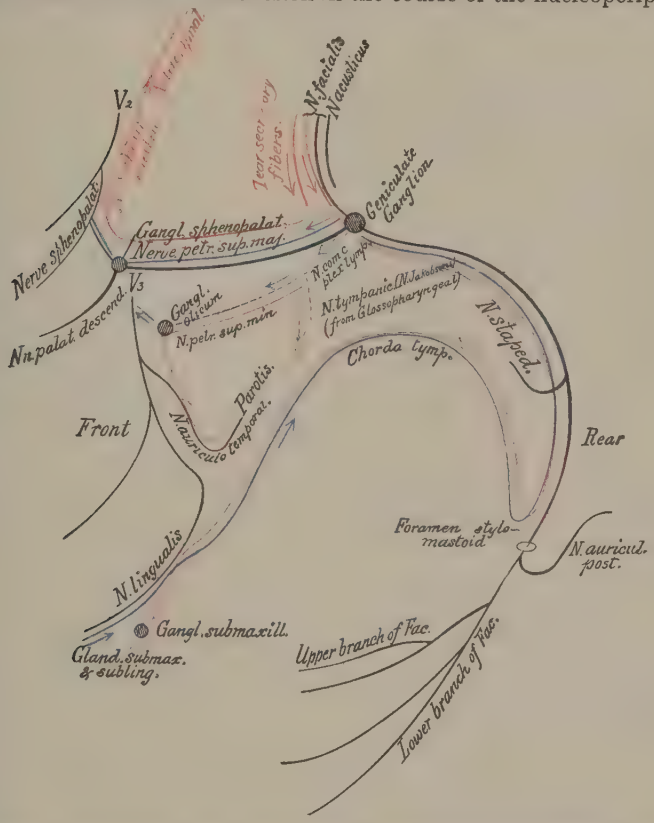


Fig. 422.—Diagrammatic plan of the peripheral facial nerve and its connections with other nerves:

——— Motor fibers of facial.
——— Other cranial nerves.
——— Secretory fibers of the facial to the submaxillary and sublingual glands and of the glossopharyngeal to the parotid.
——— Taste-fibers of the facial from the chorda tympani.
-------- Central course of the same from the geniculate ganglion according to another less probable theory. (Termination through the nervus tympanicus (Jacobson's) in the glossopharyngeal or through the otic ganglion in the third branch of the trigeminal.)

tract. This is best accomplished by referring to the diagrams (Figs. 421 and 422). Fig. 421 serves for general orientation; Fig. 422, for a comprehension of the anastomoses of the facial nerve.

In Fig. 421 it is evident that a lesion situated at *a* will affect only the so-called mimic branches of the facial, including the platysma myoides; if it be situated at *b*, above the exit of the facial from the

stylomastoid foramen, the posterior auricular nerve will also be paralyzed (this supplies the occipital muscle and the attolens, retrahens, and transversus auricular muscles).[1] As many people cannot move these muscles voluntarily, paralysis of them is oftentimes shown only by an electric examination, and then, of course, only when the electric irritability of the paralyzed muscle has been impaired. If the lesion be situated at *c*, the taste and the salivary secretory fibers of the chorda tympani are also paralyzed. This becomes evident in a diminution of the trigeminus taste appreciation upon half of the tongue in its anterior portion and possibly in a dryness of half of the mouth. (See p. 1071 for a more exact method of testing this function.) The sensations of touch and pain in the anterior half of the tongue are sometimes diminished, since the chorda tympani also contains fibers for the appreciation of touch and pain in the tongue. With a lesion at *d*, the stapedius muscle, supplied by the stapedius nerve from the facial, shares in the paralysis. (See above, p. 1070, in relation to phenomena so caused.) Should the lesion be situated still farther above at *e*, that is, above the geniculate ganglion, the disturbances of taste just mentioned escape, because the taste-fibers have left the facial at this point, but half of the palate will be paralyzed to voluntary and to reflex (see p. 1075) impulses, and the secretion of tears (see p. 1071) may be affected. Disturbances of hearing from an extension of the process to the cochlea may result from lesions in the neighborhood of the geniculate ganglion. (See p. 1072.) If the lesion be situated at *f*, at the base of the brain, where the acoustic and facial nerves are so closely approximated, the former is oftentimes involved with the latter, and in addition to the involvement of the tear secretion, diminution of hearing and disturbances of equilibrium from lesions of the fibers of the ramus vestibuli are added to the symptoms of facial paralysis. The changes in the cutaneous secretion on the side of the facial paralysis mentioned on p. 1072 have no diagnostic importance, because they may either be absent or present in any situation of the lesion. When the lesion is localized still higher up (*i. e.*, is nuclear) (*bulbar paralysis*), the coincident involvement of other bulbar nerves, the bilateral character of the paralysis, and the very unequal involvement of the individual branches of the facial make the picture sufficiently characteristic. In bulbar paralysis the territory of the lower facial (see p. 1064) is most affected, especially the lip musculature. The facial palsy due to a lesion in the pons, another nucleoperipheral palsy, since the peripheral motor neuron is also affected, is usually characterized by paralysis of the extremities upon the opposite side (alternating or crossed paralysis). This is due to the involvement of the psychomotor tract for the extremities (the pyramidal tract) before its decussation, although at this point the facial fibers have already crossed. Between this location and the cortex is the region for central facial paralysis.

In addition to these local diagnostic points (in regard to the special symptomatology of nucleoperipheral facial paralysis), the following facts will be of assistance in completing the clinical picture:

Lagophthalmus, due to paralysis of the eye branch, is a very characteristic sign in most cases of peripheral facial paralysis, and one which furnishes a sharp contrast to central facial paralysis. This con-

[1] According to Heitzmann, the attrahens auricular muscle is supplied by the auriculotemporal nerve from the third branch of the trigeminus.

sists in the eye on the paralyzed side remaining open during sleep and despite attempts to close it. In fruitless endeavors to close the eye the globe assumes the so-called sleeping position, upward and outward, more rarely upward and inward, beneath the upper lid, so that patients believe that they have completely closed the eye.

This so-called "*Bell's phenomenon*," just described, is to be attributed to an associated movement of the globe, whose object is to protect the eye. It occurs physiologically, as is shown by its appearance during sleep in a healthy individual, as well as by the fact that it also occurs when a healthy person attempts to close the eye when the closure is mechanically prevented.[1] The sign is more evident in paralysis of the eye branch of the facial, not only because the eye remains open, and so we see it more plainly, but also because the movement appears to be increased, probably because, after interruption of conductivity in the domain of facial branches, the motor impulses radiate more intensely through the pathway of the associated movement in a way quite analogous to other associated movements. Bell's phenomenon has some prognostic significance, as one of the earliest signs of improvement in facial paralyses is a retrogression of this sign. This is probably to be attributed to an improvement in the conduction function of the facial fibers, whereby a smaller proportion of the motor impulses are diverted into the branch for associated movements; with this improvement of transmission the strength of the motor impulses, corresponding to the better effect, is diminished.

[Instead of Bell's phenomenon, another very interesting condition has been observed in these cases. It consists of jerky, irregular oscillations of the eyes in a horizontal plane when forcible closure of both lids is attempted. We have as yet no satisfactory explanation for the condition, although some writers believe it due to irritation of the sixth nerve nucleus.—Ed.]

Although patients with peripheral paralysis protect themselves against a painful sensation caused by touching the cornea, nevertheless the usual lid closure (corneal reflex, p. 1062) either fails entirely or occurs very incompletely. On the contrary, automatic winking is retained. (See p. 1064.)

The true corneal reflex must not be confused (although the mistake is common) with the ordinary eye closure excited reflexly by the visual appreciation of an approaching object, even before the cornea has been touched. This latter is really an opticofacial reflex, *i. e.*, the optic nerve constitutes the sensory limb; and physiologically it is a most useful process, since it frequently protects the eye by closing the lid in time to prevent the injury, whereas the true corneal reflex would occur too late to be of any service. The optic reflex, like the genuine corneal reflex, is evidently either lost or diminished in peripheral facial paralysis. It is of some diagnostic importance in determining the condition of the facial in those cases where the true corneal reflex is absent as a result of anesthesia of the cornea (sensory trigeminus paralysis).

When a lesion is situated at *e*, the palate reflex may be lost. This can be recognized by tickling the patient's pharynx with a brush, although in unilateral facial paralysis it is often very difficult to be sure of it, as the paralyzed half is displaced toward the healthy half of the palate; in which case the displacement is often the only sign of the paralysis of the reflex.

Peculiar appearances of irritation are not infrequently observed in the partially paralyzed territory of old severe peripheral facial paralyses which have recovered completely. These consist either of contractures, which may lead to the erroneous supposition of a facial paresis of the opposite side, or of associated movements and of fibrillary contractions in the paretic and atrophic territories.

[1] This is most readily observed when one tries to keep awake in the presence of others.

Hitzig assumes that these phenomena depend upon a change in the irritability of the facial nucleus as a result of degenerative processes proceeding from the periphery, an hypothesis which coincides with Darkschewitsch's studies. The latter has discovered that peripheral lesions of the motor nerves lead to changes in the nuclear cells. These irritative phenomena in the facial territory may persist through life.

The electric irritability is generally altered in nucleoperipheral facial paralyses. In mild cases there is a more or less diminished excitability, and in severe cases a complete or partial reaction of degeneration, resulting in a degenerative atrophy of the paralyzed muscles. (See p. 1025.)

Severe peripheral facial paralyses commonly lead to vasomotor phenomena, as shown by the occurrence of coolness, cyanosis, and frequently some edema of the affected side. It has not yet been accurately determined whether this depends upon a connection between the peripheral facial and the vasomotor, or upon a lesion of the sympathetic fibers which are united to the facial branches in the periphery. Neither hypothesis is absolutely necessary, since the muscular action of the affected side is sufficiently impaired to produce some stasis (p. 1008 et seq.).

The *diminished sensibility of the affected half of the face*, not infrequently observed in facial paralysis, has led to various hypotheses. Some writers, contrary to the general opinion, assume that the facial contains some sensory fibers. This is, however, unnecessary in order to explain the disturbances of sensibility, for certainly sensory trigeminus fibers do anastomose at the periphery with the facial, and these may quite well be injured by the same cause. The absolute immobility of the affected half of the face and the associated circulatory disturbances are alone sufficient to dull the sensibility. Such disturbances are most frequently discovered while the muscles are being tested by the electric current; for this procedure is found to be more painful upon the healthy side, especially in severe paralysis, than upon the injured side. The observation certainly suggests that the degeneration of the muscles may alone be responsible for a disturbance of the sensory nerve terminations. In many cases an hysteric cause may explain the disturbance.

The *pains* accompanying rheumatic facial paralysis in the affected half of the face are probably due to coincident involvement of the peripheral trigeminus fibers running with the facial.

[At the Boston meeting of the American Neurological Association, 1906, J. Ramsay Hunt described a condition accompanying facial palsy which he considered the result of an herpetic inflammation of the geniculate ganglion. His very excellent description of this condition also contains the published cases in which herpetic vesicles had been considered coincidental. Hunt insists, however, that there is a definite syndrome, consisting of intense neuralgic pains in the ear, radiating over the face, tinnitus, vertigo, and frequently diminished hearing. An herpetic eruption soon appears on the concha, tragus, external auditory canal, or tympanic membrane; it is often very transitory and disappears rapidly, but is sometimes quite severe. At the outset there is usually a definite diminution in sensibility over the tympanic membrane and anterior surface of the external auditory canal, which, as a rule, lasts only a few days, and if the case be not seen early, will be missed or overlooked. The facial palsy which follows is of the peripheral type and generally very severe. Hunt believes that this condition establishes the fact that the seventh is a mixed nerve, and that its sensory part, which consists of the geniculate ganglion and the pars intermedia of Wrisberg, is distributed over the tympanum anterior wall of the external auditory canal and concha. The geniculate ganglion is ontogenetically the analogue of the Gasserian and spinal ganglia, and hence it is subject to the same conditions that govern herpetic inflammations elsewhere. The intimate connection of this ganglion by means of the petrosals with the auditory ganglion, Meckel's ganglion, the otic ganglion, and the Gasserian readily explain the vertigo, deafness, tinnitus, and pain radiations. A. S. Taylor and L. P. Clark presented a case at the meeting of the American Neurological Association, 1909, which seems to confirm Hunt's views, at least in part. The case was one of severe obstinate otalgia, which had been completely relieved by cutting the auditory, pars intermedia, and most of the facial nerve at the cranial opening of the Fallopian canal. The relief has been permanent thus far.

(Almost two years.) His views on the peripheral sensory distribution, however, were not confirmed, since at no time subsequent to the operation were they able to demonstrate anesthesia of the concha, anterior wall of the external auditory canal, or tympanum.—Z.]

Bulbar paralysis, which, as has been already mentioned, includes a partial nuclear facial paralysis, sometimes causes an *increased salivary secretion;* and this is peculiar in as much as there is actually more saliva secreted than normally, and not merely an excessive flow on account of imperfect closure of the lips. We may assume that this increased secretion falls under the heading of a so-called paralytic secretion. Physiologists have noted it in animals after they have cut the several nerves leading to the submaxillary glands. Such an assumption seems permissible, because the fibers supplying the sublingual and submaxillary glands really come from the glossopharyngeal, which is also involved in bulbar paralysis. Against it is the fact that experimental paralytic secretion is rather a transitory condition, and even if continued, is never very decided. The more rational explanation seems to the author to be that the swallowing mechanism is affected in bulbar paralysis, the saliva accumulates in the mouth, and its presence reflexly stimulates the secretion.

(*b*) Spasms of the Facial

Spasms in the facial territory are not rare, but their description belongs to special pathology, so that here we need only mention their occurrence in tetanus, tetany, epilepsy, facial tic, and chorea. The peculiar twitching of the lid depending upon fibrillary contractions of the facial is of some diagnostic interest. It occurs in neurasthenics when they attempt to close the eyes at command. Such an attempt, as has been frequently noted, causes some degree of difficulty in many cases. This twitching is quite an important sign of neurasthenia. Irritative appearances in the territory of old facial paralyses have been mentioned in preceding paragraphs (p. 1076 et seq.).

EIGHTH CRANIAL NERVE; AUDITORY (Acusticus)

Paralysis of the Auditory Nerve

Auditory paralyses occur in diseases of the internal ear, of the petrous bone, in affections of the base of the brain and of the medulla oblongata, and finally as a part of cerebral hemianesthesias.

A unilateral acoustic paralysis in hemianesthesia is never absolute except in hysteric affections; there is more apt to be only a moderate impairment of hearing. This may be accounted for by the fact that the central innervation of the acoustic is not entirely crossed, and coincides with the fact that in unilateral lesions of the auditory center, situated in the temporal lobes, no instance of complete crossed deafness has as yet been observed. Whereas, Wernicke has shown that a bilateral lesion of the temporal lobes can produce bilateral deafness.

In examining the auditory nerve, a procedure which should, of course, be carried out in as quiet a room as possible, the perception of sound by air conduction must be sharply distinguished from that by bone conduction. In testing the former, a ticking watch or vibrating tuning-fork is held near the external auditory canal, the maximum distance determined at which one or both can be heard, and the two sides then compared. In testing the latter, the perception of sound by bone conduction, the watch or the shank of a tuning-fork is held upon the mastoid process, and any difference between the two sides determined from the patient's statements. Since neither watches nor tuning-forks emit sounds of definite intensity, Politzer[1] has constructed an acumeter with which a sound of constant intensity may be produced by allowing a small hammer to fall upon a metallic bar. Politzer's acumeter may be employed to test the perception not only of sounds transmitted

[1] Politzer, Lehrb. der Ohrenheilkunde, Stuttgart, 1887.

through the air, but also of sounds conducted by bone, in which case the instrument is brought into contact with the cranial bones by means of a rod-shaped attachment.

Rinne's test is also of some importance. It consists in holding a vibrating tuning-fork to the mastoid process, until the patient can no longer appreciate any sound; then the tuning-fork (which is still vibrating) is quickly approached to the external ear. If the auditory transmitting apparatus be functionating well, the tuning-fork is heard again (positive result of Rinne's test); should this not be the case (negative result of Rinne's test), there must exist some disease of this apparatus. If the test be positive, the transmitting apparatus is not necessarily perfect, because air conduction permits a better auditory impression than bone conduction, and slight affections of the sound-transmitting mechanism might escape notice.

To determine a disturbance of hearing independent of the otoscopic findings and Weber's and Schwabach's tests (see below), Rinne's test must be employed in a more exact quantitative manner, by determining the degree of superiority of air-conduction over bone-conduction, by measuring the time during which a vibrating tuning-fork is heard at the external auditory meatus after it has become inaudible upon the mastoid process. Under normal conditions this time for an A tuning-fork amounts to about thirty seconds. If Rinne's test give a negative result, we may proceed in the opposite manner, by determining the time during which the tuning-fork upon the mastoid process is heard after it has become inaudible when held in front of the external auditory meatus.

Zimmermann has recently objected to the principles involved in Rinne's test, believing that in placing the tuning-fork upon the bone we test the energy of movement of the handle of the fork, and that in holding the tuning-fork at the external auditory meatus we test the much greater energy of movement of the prongs. From this he concludes that the diagnostic importance of Rinne's test is doubtful and that the normal positive result cannot be employed as an argument for Helmholtz's theory, according to which the membrana tympani and the auditory ossicles are assumed to aid in the transmission of sound. According to Zimmermann's theory (see p. 1070 et seq.), the normal positive result of Rinne's test is due to the fact that the auditory ossicles may really be an accommodation mechanism for the acoustic organ, or, in other words, a sound-dulling, rather than a sound-transmitting, apparatus. These views of Zimmermann have been successfully combated by v. Bezold, who has suggested a new method of performing Rinne's test. Performed in this way, the test is free from objection and rehabilitates Helmholtz's theory. He provides the A tuning-fork with a rounded handle, and after the vibrations have become inaudible, both upon the mastoid process and at the external auditory meatus, he introduces this handle into the meatus, so that an air-tight closure of the canal is effected. It then becomes manifest that the audibility of the tuning-fork, introduced in this manner, is increased on the average by about twelve seconds over the ordinary perception by means of air-conduction; the vibrations are consequently perceived by air-conduction about thirty plus twelve seconds longer than by bone-conduction (the normal positive result of Rinne's test carried out in this manner). In this test air-conduction and bone-conduction are both measured with the handle of the fork, so that the results may be absolutely and directly compared.

The so-called *Weber's test* has a similar significance for the differentiation of impaired hearing due to disturbances of the conducting apparatus from that dependent upon affections of the nervous portion of the acoustic organ. The handle of a vibrating tuning-fork is placed upon the middle of the vertex, and the patient is required to state upon which side he perceives the louder sound. In affections of the conducting apparatus the sound is usually more distinctly perceived upon the affected side, because less energy is dissipated externally through the drum membrane, while the reverse is true in affections of the auditory

nerve or of the labyrinth. The chief objection to Weber's test is the uncertainty of the localization of the auditory perception in one ear.

Schwabach's test consists in determining whether the vibrating tuning-fork is perceived by bone-conduction for an abnormal period of time. If it be heard longer than normal, Schwabach supposes a disturbance of the conducting apparatus; if not so long as normal, an affection of the nervous mechanism. (The explanation is the same as in Weber's test.) If the investigator be possessed of normal hearing, this comparison is best made by removing the tuning-fork from the patient's mastoid process as soon as he declares it to be inaudible, and placing it upon the mastoid process of the investigator; the result is then to be compared with that obtained by reversing the process.

The results of all these tests, however, should be utilized with caution, since the pitch and intensity of the sound employed may sometimes cause them to vary and even be the direct opposite of what the formulated rules would lead us to expect.

The usual method adopted in ear clinics for testing the auditory nerve is to determine which of a series of tuning-forks, comprising the entire tone scale, can be appreciated. This method has not yet been adopted in internal medicine, because only gross disturbances can be utilized in the local diagnosis of cerebral diseases.

More recently, the reliability of this method has been questioned, because its theoretic basis (namely, that for the perception of the tuning-fork vibrations only the fundamental tones and no over tones come into consideration) seems to be inadequate. In spite of this, the method of testing with the tuning-fork series has given the practical and important result that in diseases of the middle ear a constant limitation of the tone perception is found in the lower scale; whereas in diseases of the internal ear and in old age, defects are found more commonly in the upper register.

Von Bezold[1] recommends, in place of the continuous series, one or two of the lower (weighted) forks (those which read the tones G_2– – – – D_1 and D_1– – – – A_1) and the use of the Galton whistle for the higher tones.

The acuity of hearing should be tested by means of the whispered voice, as well as by means of the above-described instrumental test. In a quiet room the examiner notes at what distance from each ear (the other being closed) the whispered voice can be heard; experience has shown that such a method frequently furnishes quite different results from the instrumental test. The whispered voice is preferable to the loud voice, not only because the latter would be too intense in a closed space, but also because the individual sounds and words are more uniformly adapted for auditory perception when whispered than when loudly spoken.

Irritative Phenomena of the Auditory Nerve

Subjective sound phenomena result from various cerebral diseases, from galvanic stimulation of the brain, and especially from affections of the internal and middle ear. The most familiar are the ear noises heard in chronic sclerotic otitis media, the "crux" of the otologists. This acoustic phenomenon of irritation does not possess in cerebral disease any very important local diagnostic significance, because even the most exact otoscopic examinations cannot differentiate with certainty the subjective perceptions of peripheral from those of central origin. A peripheral origin is much more probable, on the one hand, on account of the great frequency of middle-ear diseases, and, on the other hand, on account of the generally applicable law that the terminal organs of sensory nerves are the most irritable parts of the sensory apparatus. Pathologic appearances of the drum argue for a peripheral origin of the ear noises. A normal drum, however, does not necessarily exclude such an origin.

Auditory Vertigo (*Ménière's Disease*).—Since the vestibular branches of the acoustic nerve supply the semicircular canals, and since the latter are regarded as the organs of equilibrium, it is easy to understand that vertigo will result from affections of the acoustic nerve. Vertigo is, in fact, most commonly observed accompanying affections of the labyrinth and of the middle ear. (In regard to this, see chapter on Vertigo, p. 1092.)

Otoscopic Examinations

Disease of the auditory apparatus is frequent, even in people who consider themselves perfectly well. Hence, under all circumstances in

[1] Von Bezold, Lehrb. der Ohrenheilkunde, 1906.

which a disturbance of hearing has been determined, it is important to make an otoscopic examination. In no other way can we differentiate between disturbance of hearing dependent upon disease of the auditory nerve and that due to disease of the ear itself. This distinction, as was mentioned above, cannot always be determined by the Rinne test, even when conducted according to von Bezold (p. 1078). Weber's and Schwabach's tests (see p. 1079) also give at times uncertain results, and in some instances even an otoscopic examination fails, so that a disturbance of hearing will not always assist much in the diagnosis of cerebral disease.

The reader is advised to consult the otoscopic pictures in Politzer's Atlas der Beleuchtungsbilder des Trommelfells, Wien, Braumüller, 1896, and von Bezold's Lehrbuch der Ohrenheilkunde, Wiesbaden, Bergman, 1906.

Demonstration of Simulated Deafness[1]

Simulation of total deafness of both ears may usually be detected merely by prolonged observation of the patient in a hospital.

The *simulation of bilateral or unilateral impairment of hearing* becomes evident when we test the patient's hearing (that of each ear) with his eyes closed, so that he cannot see the distance from which the sound comes. He will then express contradictory statements in regard to rapidly repeated tests.

Simulation of unilateral total deafness may be discovered in various ways:

1. The patient's normal ear is closed, and the examiner speaks directly in front of the supposedly deaf ear. If the patient claim not to hear this, either simulation or exaggeration exists, because under such conditions even the closed healthy ear would appreciate the conversational voice.

2. One end of a flexible rubber tube, about 4 feet long, is inserted into the external canal of the patient's ear; another similar tube into the other ear. Funnels are affixed to the other end of each tube. The examiner, speaking in a whisper behind the patient, talks at one moment into the one, and at another moment into the other, funnel, alternating as quickly as possible, and the patient is required to repeat what is said. In consequence of the confusion and the fatigue which this process produces, if simulation exists, the patient finally repeats what is spoken into the supposedly deaf ear. The examiner must be trained for the test. The best plan is to write down beforehand what is to be said in two columns, one marked L for the left ear, and the other R for the right ear. This procedure is to a certain extent analogous to the stereoscopic method of investigating simulated unilateral blindness (p. 1038).

3. An A tuning-fork is set in vibration and placed vertically upon the middle of the skull; if even one ear be normal, the patient must hear the tone. The test is then repeated with the normal ear closed, and if the patient says that he no longer hears the tone, it is evident that he is simulating, since by bone conduction the normal ear, even if it be closed, must hear the tuning-fork.

4. Many malingerers are exposed by the fact that they insist upon their inability to determine whether the tuning-fork vibrates or not,

[1] Partly taken from Siebermann, Untersuchung auf Simulation von Schwerhörigkeit oder Taubheit, Schweizerischer Medicinalkalender, 1895, p. 76 et seq.

when the examiner places a large vibrating tuning-fork (A or C or A) upon the skull in the neighborhood of the supposedly deaf ear, whereas the vibrations of such a type of tuning-fork can be felt even by the deaf.

Siebermann quite correctly calls attention to the danger of confusing exaggeration and complete simulation, and emphasizes the advisability of never placing any reliance upon the results of one method of examination.

In regard to the demonstration of the simulation of disturbances of hearing, the reader is referred to Burchardt's work, referred to upon p. 1039.

NINTH, TENTH, ELEVENTH CRANIAL NERVES: GLOSSOPHARYNGEAL, VAGUS, SPINAL ACCESSORY (VAGUS GROUP)

Physiology

These three nerves are so intimately connected at their origin in the oblongata, both during and after their exit from the jugular foramen, and they possess so many anastomoses, that experimental physiology has not yet succeeded in isolating the functions of each. This is especially so in the case of the vagus and spinal accessory. Clinical investigations are made exceptionally difficult, because, as a result of the anatomic relations of these nerves, pathologic conditions frequently affect the three simultaneously, both centrally and peripherally.

The *peripheral glossopharyngeal nerve* supplies *motor fibers* to the muscles of the pharynx, to the pharyngeal constrictors, and to the stylopharyngeus muscle; and it participates with the facial and the accessory in the supply of the muscles of the soft palate. In addition the glossopharyngeal is the *secretory nerve* of the parotid gland. From the petrous ganglion it gives off these secretory fibers through the tympanic nerve (Jacobson's) to the otic ganglion, and from there by means of the auriculotemporal nerve of the third trigeminal branch to the parotid gland (Fig. 422, p. 1073). The glossopharyngeal also contains *sensory fibers*, which are distributed to the back of the tongue, to the pharynx, and to the soft palate. These fibers convey impulses for the sensation of taste (*i. e.*, for bitter and sweet), and they also inhibit breathing during the act of swallowing.

The *peripheral vagus* includes both motor and sensory fibers. The *motor fibers*, together with those of the glossopharyngeal and accessory, supply the muscles of the pharynx, the soft palate, and the esophagus, so that the vagus, with the glossopharyngeal, plays an important part in the act of swallowing. In addition it furnishes motor fibers to the larynx through its inferior or recurrent laryngeal branch, and there supplies all the laryngeal muscles, except the cricothyroid and the two epiglottis muscles (the thyro- and aryteno-epiglottis). The last three, although not innervated by the recurrent laryngeal nerve, are supplied by fibers derived from the vagus, through the superior laryngeal nerve, which, therefore, innervates the cricothyroid muscles and the muscles of the epiglottis. The vagus is furthermore the motor nerve of the stomach and of part of the intestines; it is also the inhibitory nerve of the heart, for, as is well known, a centrifugal irritation of one or both vagi slows the action of the heart and at the same time diminishes the cardiac power, whereas sectioning one or both vagi increases the heart-rate. The vagus is further assumed to innervate the bronchial muscles and the vessels of the lungs. Sensory branches: It gives off a *small sensory branch* (auricular branch of the vagus) to the posterior wall of the external auditory canal. The mucous membrane of the pharynx larynx, trachea, and bronchi is supplied by the vagus, as well as the heart and probably also the stomach and intestines. The sensory nerves for the upper part of the larynx run in the so-called *superior laryngeal branch*, those for the lower part of the larynx in the *inferior* or *recurrent laryngeal*. The sensory fibers of the vagus exert an important regulatory control over the breathing; their best-known effect is shown by centripetal stimulation of the superior laryngeal—the respiration ceases in the expiratory phase. The sensory vagus branches to the lung itself influence breathing to the extent that distention or inflation of the lung excites expiration, while compression or collapse of the lung excites inspiration. The automatic regulation of breathing, as explained by Hering and Breuer, should be understood to mean merely that by sensory irritation of the pulmonary branches of the vagus an

attempt is made to establish a median position of pulmonary distention, whereas the rhythm of breathing is independent of such regulation, being rather an automatic function of the respiratory center. In reality the only influence that the centripetal vagus fibers have upon the rhythm is that sectioning the vagus slows the respiration, while weak centripetal vagus irritation increases the rate. The vagus is the most important sensory nerve for coughing, which can be induced by any one of its sensory branches (even including the auricular branch). The vagus branch coming from the heart, which can be demonstrated in animals, is called the *Ludwig-Cyon depressor*. It is of some clinical interest, because its centripetal irritation produces a marked diminution of blood-pressure without affecting the heart, probably from vascular dilatation.

The peculiar sensation of nausea and the reflex vomiting depending upon such sensation may start from the sensory branches of the vagus to the pharynx and stomach. Vomiting does not, however, depend upon intact vagi, for in animals the vomiting paroxysm can still be excited from the stomach, even after bilateral section of the vagus. Other tracts for the vomiting reflex probably must exist, although they are unknown. The vagus is supposed to have some *secretory influence*, especially in the stomach, but it has not yet been definitely demonstrated.

The functions of the *peripheral spinal accessory nerve* are simple; they are purely motor. Its *internal branch* anastomoses with the pharyngeal branches of the vagus and the glossopharyngeal, thus sharing in the motor innervation of the soft palate, while its *external branch* supplies the sternocleidomastoid and trapezius muscles.

The determination of the central origin of fibers which control individual functions is much more difficult than the study of the peripheral branching and functions of these three nerves. Two points are sure—that the taste-fibers are derived from the glossopharyngeal nucleus, and that the innervation of the sternocleidomastoid is exclusively a function of the accessory nucleus. From reasons which have been detailed above (p. 1081), we are still undecided whether many functions executed in the peripheral tracts of the vagus and glossopharyngeal are not controlled by fibers which in reality are derived from the accessory nucleus, but which at the periphery are associated with the two other nerves. For instance, the heart-accelerating fibers of the vagus, and especially the motor fibers for the larynx, are supposed by many writers to be derived from the accessory nucleus. Grabower, however, has recently denied this relation of the accessory to the larynx. At all events the question is not settled. Nor is it yet possible to state with certainty how far the accessory nucleus shares in the innervation of the glossopharyngeal and vagus fibers which supply the swallowing and palate musculature.

In regard to the anatomic relations of the nuclei of the three nerves of the vagus group, see Figs. 430 and 431.

Pathologic Relations

The fibers of the three nerves of the vagus group may be affected either in their peripheral course or within the cranium, *i. e.*, in the medulla oblongata. The same peculiarities are true in regard to their central (supranuclear) innervation, as in the case of the nerves to the ocular muscles, of the motor trigeminus, and of the superior branch of the facial, viz.: that their central innervation is not exclusively contralateral, but that the hemisphere of each side takes part in innervating the two nerves. (See Fig. 403, p. 1041.) As a result, lesion of one hemisphere occasions very little or no disturbance in the nerves of the vagus group, because the other hemisphere then performs the function sufficiently well; and, therefore, without further discussion unilateral affections can, for the most part, be attributed to a lesion at the base of the brain or in the oblongata, provided, of course, that the trouble is situated within the skull. This is exactly the same condition as in unilateral paralysis of the eye muscles (see p. 1040 et seq.) and motor paralysis of the trigeminus (p. 1061). With a cerebral hemiplegia, such as is usually localized in the cerebrum, there is practically never any disturbance of the vocal cords, of the muscles of swallowing, nor of the sternocleidomastoid, whereas a paresis of the trapezius is regularly noticed upon the

hemiplegic side, because the innervation of this muscle is, for the most part, crossed. The clavicular portion of the trapezius, however, which aids in respiration, is bilaterally innervated and so exempt from this paresis. A bilateral paralysis of the nerves of the vagus group may, of course, originate from bilateral hemisphere lesions as a "pseudobulbar" condition. (See p. 1090.)

Symptomatology of Lesions of the Three Nerves of the Vagus Group.—Disturbances of the motor innervation of the soft palate may occur in paralysis not only of the facial, but also of the glossopharyngeal and vagus, as well as of the nuclear and trunk portions of the accessory, and, according to p. 1061, of the motor trigeminus. In regard to the phenomena of unilateral or bilateral paralysis of the palate, see the section upon the facial nerve (see pp. 1063 and (reflex) 1075), and p. 1062 in regard to the influence of the trigeminus. In a similar way the peripheral glossopharyngeal and vagus, and even the region of origin of the accessory, are to be considered in connection with the other movements of swallowing. A patient's subjective complaints and the examiner's observation of the act of swallowing, will disclose any affection of that function. A unilateral vagus paralysis, such as is observed after injury, does not noticeably affect swallowing. Disturbances in the motor innervation of the larynx, proceeding from the vagus or the accessory, become evident either during phonation, or by the exhibition of deficient laryngeal closure or laryngeal stenosis (in posticus paralysis, see below). Imperfections in phonation depend upon a lesion of fibers running to the vocal cord musculature in the inferior laryngeal nerve. Deficient closure of the glottis depends upon a paralysis of the glottis constrictors (crico-arytenoideus lateralis and interarytenoidei), as well as of the aryteno-epiglottis. The two former are supplied by the inferior laryngeal and the latter by the superior laryngeal nerve. The consequence of deficient laryngeal closure is that patients readily choke in swallowing, and can no longer effectually cough or strain. Traube has proved that paralysis of the glottis closure, with inability to cough and expectorate, is the most essential cause of the disastrous results (vagus pneumonia) of bilateral section of the vagus in animals and of bilateral vagus paralysis in men. Whether or not paralysis of the bronchial muscles and of the pulmonary vessels plays any rôle in this is not yet accurately determined. In unilateral vagus paralysis phonation and glottis closure are not always so markedly affected as one would think, because a more pronounced movement of the healthy vocal cord will, to a great extent, compensate for the paralyzed cord. Still, the hoarse, feeble voice of complete unilateral vocal paralysis is so very characteristic that such a diagnosis may sometimes be made, even before a laryngoscopic examination, providing the other clinical symptoms suggest it. A gradually developing paralysis of the recurrent nerve (whether this be of peripheral or of nuclear origin) almost always involves the crico-arytenoideus posticus first. This muscle widens the glottis. Hence, the earliest symptoms of an increasing motor laryngeal paralysis is a narrowing of the glottis, because the constrictors overpower the weakened posticus. The corresponding vocal cord assumes a position of adduction. Should the paralysis be bilateral, there may result a serious obstacle to breathing, with all the symptoms of laryngeal stenotic dyspnea (see p. 93 et seq.), even necessitating tracheotomy. Such a condition is generally described briefly as "posticus paralysis."

This remarkable selection of the crico-arytenoideus posticus in the beginning of recurrent paralysis has led to countless discussions. No satisfactory explanation has yet been given. One theory is that those neurons which preside over glottis widening suffer on account of a greater sensitiveness, but this seems to the author arbitrary and superfluous. A much simpler explanation is that, quantitatively, the musculature of the glottis constrictors overpowers the dilators very decidedly. This preponderance is in keeping with the fact that in phonation. coughing, straining, and, in short, in all forms of glottis closure, the constrictors accomplish very much more than the dilators. As a matter of fact, all laryngeal muscles, with the single exception of the crico-arytenoideus posticus, subserve the function of narrowing the glottis, and, therefore, it is not surprising that this muscle is the first to suffer, and that in partial laryngeal paralysis the constrictors overpower it. Evidently, as the paralysis increases, the narrowing of the glottis becomes less marked, while the vocal cord (or cords) from a position of adduction assume more and more the so-called cadaveric position. (See Fig. 341, p. 900.) The exact diagnosis of a motor laryngeal paralysis can only be made with the help of the laryngoscope. (See the chapter upon Laryngoscopy and the illustrations of the larynx reproduced there, p. 900.) A normal laryngoscopic picture is characteristic of hysteric aphonia: the larynx resembles that of a person voluntarily whispering. There is no actual paralysis in the territory of the vagus and accessory, but merely a psychic inability to control the speech. Spasm of the glottis and the spastic form of hysteric aphonia may be mentioned here, as motor vagus accessory symptoms; but for their explanation the literature of special pathology should be consulted.

See p. 1062 et seq. (trigeminus) concerning derangements of taste peculiar to lesions of the glossopharyngeal (especially for bitter and sweet). Affections of the sensory innervation of the larynx (superior and inferior laryngeal nerves) can be demonstrated by touching the mucous membrane of the larynx by means of a curved laryngeal sound, under the guidance of a mirror, and noting the absence of sensitiveness, and even the loss of the cough reflex.

The determination of disturbances in function of the cardiac and pulmonary branches of the vagus is usually very difficult, because all the circulatory and respiratory changes produced by irritation and paralysis of this nerve may arise pathologically in other ways, especially in affections of the heart and of the lungs themselves, and also reflexly from almost any nerve territory. The establishment of less ambiguous symptoms, especially the determination of the phenomena described above in connection with the act of swallowing and the laryngeal innervation, as well as the establishment of lesions whose nature and position can be definitely attributed to the vagus, will generally be sufficient to attribute certain respiratory and circulatory disorders to paralytic or irritative vagus phenomena. The cases of traumatic vagus paralysis are the easiest to understand.

The results of surgical or other accidents, such as cutting the vagus nerve during operations, or the results of injury to both vagi from the pressure of tumors, prove that a unilateral vagus paralysis need not influence the pulse very materially. At first it may be accelerated, but later on it will become equalized. A double vagus paralysis will, however, generally induce a permanent acceleration, up to 160 beats in a

minute. Dilatation of the heart has not yet been observed as a result of unilateral or bilateral vagus paralysis; nor is there any foundation for the frequent assumption that irregularity of the pulse is to be attributed to paralyzing affections of the vagus. On the contrary, physiology teaches that irritation of the vagus may cause irregularity in the pulse.

The rule formulated by Gerhardt in connection with the diagnosis of the cause of *tachycardia* should be mentioned here: "Taken all in all, the majority of nervous tachycardias are to be attributed to vagus paralysis, those with very rapid pulse (above 200) to a combination of vagus paralysis with sympathetic irritation, a few rather milder forms to the latter alone." Martius adds: "This rule coincides with well-known physiologic facts. In unpoisoned animals an acceleration of the heart rate of 30 to 70 per cent. (not more, Aubert) can be brought about by stimulating the accelerating nerve of the sympathetic. After bilateral sectioning of the vagus, the acceleration of the pulse-frequency in mammals is not very great. According to von Bezold it may rise to 120 to 180 beats. The following conclusions may be drawn: Acceleration up to about 120 beats (30 to 70 per cent.) depends upon irritation of the sympathetic; from 120 to 180 beats, upon paralysis of the vagus; more than that, upon a combined action of both causes."[1] Nothnagel has also made an attempt to formulate rules for diagnosticating the cause of tachycardia. He says: (1) "If a very decided acceleration of the pulse occur in paroxysmal tachycardia, if the rhythm be quite regular, and the cardiac impulse very weak, if other symptoms be either absent or only develop as consequences of incomplete systoles, if, finally, the paralysis of other nerve-tracts accompanying the vagus can be confirmed at the same time, then one can assume a vagus paralysis as a cause in this special case. (2) If during the attacks of tachycardia the cardiac impulses be vigorous, if the peripheral arteries be well filled, and the tension be preserved (but this is not in any sense a necessity), if other marked evidence of irritation in vasomotor nerve-tracts appear in paroxysms, then the assumption of a condition of irritation of the accelerating nerve (sympathetic) is justified."

Martius objects to the assumption of a vagus paralysis or of a sympathetic irritation to explain tachycardia. He assumes neither a vagus paralysis nor sympathetic irritation to interpret the characteristic clinical picture of paroxysmal tachycardia, but considers that it depends upon a temporary acute cardiac insufficiency with dilatation, in which the tachycardia is one of the secondary, or probably compensatory, symptoms. But this conception of Martius does not seem logical to the author; for in paroxysmal tachycardia evidence of cardiac insufficiency is so insignificant that in some cases one might better assume a sort of epileptic discharge in the territory of the accelerating nerve of the heart, which exert positive chronotropic influences (Engelman); and in others, on the contrary, the clinical picture of paroxysmal tachycardia apparently depends upon an accumulation of regular extrasystoles (p. 111).

The statements which are to be found in literature concerning the behavior of the breathing in vagus paralysis are of little use. According to physiologic experiments, it is fair to assume here, as with the heart, that only bilateral lesions can cause serious difficulties. Edinger's statement that vagus paralysis may be associated with pulmonary distention, and consequently with dyspnea, is worth noting. Vagus pneumonia (as we saw upon p. 1083) depends essentially upon incomplete laryngeal closure, and is, therefore, merely an indirect pulmonary symptom of vagus paralysis.

As yet there is very little known about the effect of vagus paralysis upon disturbances of the functions of the stomach and intestines in man. This alone appears certain—a unilateral vagus paralysis does not noticeably influence these functions.

We now come to the mention of the symptomatology of the affections of the so-called external branch of the accessory, which supplies

[1] Martius, Tachycardia, Stuttgart, Enke, 1895.

the sternocleidomastoid and trapezius muscles. A unilateral paralysis of the sternocleidomastoid causes a moderate twisting of the head toward the paralyzed side, associated with a slight elevation of the chin, due to the action of the antagonists. Turning the head to the healthy side, although performed less vigorously than normally, is not prevented, because this movement is accomplished not exclusively by the sternocleidomastoid, but also by the deep muscles of the neck, especially the obliquus capitis inferior, and the splenius of the other side. The clonic and tonic wry neck (*tic rotatoire, caput obstipum spasticum*) depend partly upon a unilateral irritation of the spinal accessory nerve supplying the sternocleidomastoid. Yet the unsatisfactory results following myotomies of the sternocleidomastoid alone, and the very much better results when the opposed splenius and the oblique capitis inferior have also been cut, show that the name "accessory cramp" for this condition is not absolutely justified. In reality the condition depends much more upon spasm of an extensive central area which supplies functionally related muscles. This corresponds to the modern conception of tics that they are automatisms which are developed from coördinated voluntary movements. The symptoms of unilateral paralysis of the trapezius vary according to whether the entire muscle or only separate portions of it are involved. If complete, the affected shoulder hangs lower; the shoulder-blade is thrust out obliquely forward and outward, and its inner border runs obliquely from below upward and outward. The power to lift the arm is somewhat impaired, but not nearly so markedly as in serratus paralysis. If only the central portion (acromial) be paralyzed, the upper half of the median edge of the shoulder-blade is depressed outward (*mouvement de bascule*, Duchenne). According to Schlodtmann, if the origin of the accessory be affected, this central portion of the muscle remains exempt, because it is entirely or partly supplied by the cervical plexus. This point has not yet been definitely decided, nor has the extent to which the cervical nerves assist in the innervation of other parts of the trapezius. It is worth noting that in juvenile muscular atrophy the clavicular bundle of the trapezius, whose function is essentially respiratory, remains intact longest, so that Duchenne has described it as the ultimum moriens of the muscle. In regard to the analogous behavior of this portion in hemiplegia, because of its bilateral innervation, see p. 1083.

TWELFTH CRANIAL NERVE; HYPOGLOSSUS

The hypoglossus is the motor nerve of the tongue, and, therefore, aids in chewing, swallowing, and especially in speaking. Its function is tested by observing whether coarse movements of the tongue are performed equally well upon both sides, and by watching the patient while chewing and swallowing. With a unilateral hypoglossal paralysis or paresis, the tongue, when protruded, deviates toward the paralyzed side, because the healthy genioglossus muscle overpowers its paralyzed fellow. If the action of the genioglossus be lost or impaired, the protruding action of the genioglossus of the opposite side preponderates, and the tip of the tongue deviates toward the paralyzed side.

Further evidence proving that the genioglossus muscle is at fault is furnished by observing the tongue as it rests naturally upon the floor of the mouth in unilateral hypoglossal paralysis. As a result of the greater strength of the unaffected muscle,

the tip will, in this position, be deviated toward the healthy side; and, in addition, a more prominent arching of the dorsum of the tongue will be noted upon the paralyzed side. This curving shows that the forward pull of the genioglossus has ceased.

In unilateral hypoglossal paralysis we by no means always notice any pronounced disturbance either by chewing or swallowing. Even articulation may be carried out reasonably well, especially after some practice.

In old peripheral paralyses of the hypoglossus the affected half of the tongue is flaccid, thin, and wrinkled, and often shows fibrillary contractions in the shape of peculiar peristaltic wavering. Electric stimulation of the lingual nerve (chorda tympani fibers) will oftentimes intensify this wavering so decidedly that an actual movement of the tongue occurs (pseudomotor action, Heidenhain). The tongue is frequently more coated upon the paralyzed than upon the healthy side.

With bilateral hypoglossal paralysis the disturbances of function are naturally very marked. The tongue lies flaccid upon the floor of the mouth, and can be protruded only very incompletely, if at all. Speech becomes incomprehensible, and mastication, chewing, and swallowing finally become impossible. The patient cannot even swallow the saliva, but must either spit it out frequently or drool constantly.

In a peripheral hypoglossal paralysis the muscles attached to the hyoid bone and supplied by the descending branch of the hypoglossus are also frequently involved together (sternothyroid, thyrohyoid, sternohyoid, and the inferior belly of the omohyoid). The fibers for these muscles originate in the second and third cervical nerve-roots. Part of them join the root of the hypoglossal nerve and later leave it again as the descending branch; part of them join the latter branch further down. When in conjunction with a lingual paralysis, these muscles are found to be affected, it is natural to conclude that the lesion is situated in the hypoglossal trunk below the anastomosis with the superior cervical nerves. The paralysis of the inferior hyoid muscles can be recognized by an atrophy of the musculature over the thyroid cartilage, and by a more noticeable prominence of the latter. If the paralysis be unilateral, the larynx will be seen to be dislocated laterally during the act of swallowing. Under some circumstances such paralysis may be demonstrated by an electric examination (motor points, see p. 1013, Fig. 390).

The electric examination of the tongue itself should be carried out in the ordinary way (p. 1009 et seq.). The motor point of the hypoglossus is situated just behind and above the cornu of the hyoid bone. (See p. 1013, Fig. 390.) In many individuals the nerve can be stimulated alone at this point by deep pressure of the fine electrode.

The hypoglossus of each side is innervated by both hemispheres, and, therefore, unilateral cerebral lesions causing a hemiplegia give very little evidence of hypoglossal paralysis. The same conditions apply as in the behavior of the superior facial branch in hemiplegia of or in central facial paralysis. (See p. 1066 et seq.) The crossed influence is, however, responsible for a more or less plain deviation of the tongue toward the paralyzed side in an ordinary hemiplegia, depending, as has already been said, upon a weakness of the genioglossus muscle upon the paralyzed side. This deviation of the tongue in hemiplegia ordinarily runs a parallel course with the facial paralysis, and for this reason was formerly attributed to the facial nerve. Such a supposition is, of course, incorrect. The coincidence of central facial paralysis and hypoglossal paresis depends upon the intimate proximity of the central tracts, or even of the cortical centers, of these two nerves.

Ordinarily, no particular difficulty in chewing, swallowing, or speaking results from this hemiplegic hypoglossus paresis; at most it has only a transitory effect on these functions.

II. THE CHARACTERISTICS OF MOTOR HEMIPLEGIA; PSEUDOBULBAR SYMPTOMS

In the preceding paragraphs (see the diagram, Fig. 403, p. 1041) we have emphasized the fact that most of the cranial nerves are supplied by both hemispheres, so that a unilateral hemispheric lesion producing a hemiplegia of the extremities does not cause any marked crossed paralysis of the cranial nerves. This rule applies particularly to the nerves of the eye muscles (except in the conjugate tract for the lateral movement), to the motor trigeminus, to the motor glossopharyngeal, to the vagus, and to most fibers of the accessory, *i. e.*, those to the vocal cords and to the sternocleidomastoid. As was mentioned above, a unilateral hemispheric lesion has a slight crossed effect upon the upper branches of the facial, upon the hypoglossal (genioglossus) and upon the fibers to the trapezius, with the exception of those to the clavicular portion, which remain intact. The fibers of the inferior facial branch are, on the contrary, very decidedly affected, because crossed. Therefore, the typical clinical picture of cerebral hemiplegia includes a pronounced paralysis of the muscles supplied by the lower branch of the facial, while those supplied by the other motor cranial nerves are either intact or slightly and partially paralyzed.

In a similar way the respiratory and abdominal muscles, apparently innervated bilaterally, present merely a slight negligible weakness on the paralyzed side.

A bilateral defective innervation is, however, probably present in any unilateral hemispheric lesion, but escapes notice because it is very difficult to detect any objective evidence of a moderate degree of bilateral paralysis (this was alluded to in the case of the eye muscles upon p. 1041 et seq., and is quite as true for other muscle territories innervated bilaterally).

Wernicke[1] and Mann undertook not long ago a more accurate analysis of motor hemiplegia in order to compare the degree of involvement of the individual muscles of the extremities. They demonstrated, what had been well known for a long time, that the leg is always affected less than the arm, and proximal less than distal parts, and formulated the following rules in regard to the amount of involvement of the individual muscle groups of the arm and leg.

Arm.—The movements most affected, and in milder and less distinctive paralysis oftentimes the only ones, are extension in all joints (elbow, hand, and finger joints), supination of the hand, abduction and adduction, and the opposition of the thumb, and spreading of the fingers. All other movements, especially those of flexion, are less affected. The ordinary position of the paralyzed arm is, therefore, flexed at all joints and slightly pronated.

Leg.[2]—The muscles most decidedly paralyzed, and, in milder and less distinctive paralysis, the only ones affected, are those which shorten and advance the leg in walking, *i. e.*, those which flex the leg and are thereby efficient at the first stage of the movement. The more important muscles for walking, those which elongate the leg and so push the body forward, are, on the contrary, either less paralyzed or in milder cases not at all affected. The flexors of the thighs and legs, the iliopsoas, the gracilis, the sartorius, and the dorsal flexors of the foot, *i. e.*, the tibialis anticus and extensor digitorum communis, are, therefore, conspicuously paralyzed. Although the long head of the biceps and the semitendinosus and semimembranosus can act as flexors of the leg, they are less paralyzed. This, however, does not argue against the above rule, because, on account of their extensor action upon the hip-joint in walking, they functionate not as flexors of the leg, but as extensors of the thigh; in other words, as elongators of the leg. In the same way the gastrocnemius does not act as a flexor of the leg in walking, but as an extensor of the foot, therefore, elongating the leg, and so, in accordance with the above rule, remains comparatively free in hemiplegias. It may be added that in hemiplegias, flexion of the thigh is often found to be less affected than Mann's rules would lead us to think, because the quadriceps, acting as an extensor, aids the iliopsoas in this movement.

[1] Wernicke, Berlin. klin. Woch., 1889, p. 45, and Lehrb. der Gehirnkrankheiten, Cassel, Fischer, 1881.

[2] Mann, Volkmann's Sammlung klin. Vorträge, Neue Folge, Leipzig, 1895, No. 132, and Deut. Zeit. f. Nervenheilk., 1896, vol. x, parts 1 and 2, p. 1.

To explain this peculiarity in distribution of motor paralysis in hemiplegias, which applies both to cerebral and to spinal types (see p. 1125), we may assume that the seriously paralyzed muscles, like the muscles supplied by the inferior branch of the facial, depend for their innervation upon the opposite hemisphere, whereas the groups of muscles less affected by the hemiplegia, like those supplied by the upper branch of the facial and most motor cranial nerves, are supplied by both sides, and, therefore, exhibit perhaps a weakness, but never any decided paralysis. The researches of Pitres and Dignat[1] completely corroborate this assumption of bilateral innervation, for in cerebral hemiplegias they found a diminution in the power of the healthy leg amounting to 50 per cent., in the healthy arm amounting to 38 per cent. Therefore, what we call hemiplegias are not hemiplegias at all, accurately speaking, but paraplegias with a preponderating crossed paralysis.

Fig. 423.—Left hemiplegia, showing contractures and distortion of mouth (Dr. E. G. Cutler, Massachusetts General Hospital).

The rules proposed by Mann in regard to the behavior of the elongators and shorteners of the leg frequently apply in spinal cord lesions which partially interrupt the motor conduction upon both sides (incomplete transverse lesions, motor systemic diseases). Perhaps this peculiarity may be explained by assuming that, in addition to their bilateral innervation, the elongators possess other more favorable conditions of innervation, *e. g.*, possibly a greater number of fibers in their conduction tracts, or increased capacity. If we assume that this peculiarity of bilateral innervation of muscle groups applies to the peripheral neurons also, it would signify a better innervation of the spinal reflexes, or a better tonus of these muscle groups. This, together with the explanation given on p. 954, would account for the fact that the slightly paralyzed and probably bilaterally innervated muscle groups (in the arm the flexors, in the leg the extensors) preponderate in hemiplegic contractures.

[1] Cited by Pierre Marie, Leçons sur les maladies de la moelle, 1892, p. 26.

In bilateral hemispheric lesions we observe very characteristic appearances upon the part of the motor cranial nerves, as a result of their bilateral innervation. Since each lesion affects fibers for both sides, a bilateral deficiency of innervation must result, for which there can be no compensation. A glance at Fig. 403, p. 1041 (supposing a coincident existence of lesions *x* and *z*), will make this clear. If these bilateral hemispheric areas involve especially the motor fibers, they may, by combination, cause a marked bilateral paralysis of those motor cranial nerves which would not be conspicuously paralyzed were the trouble unilateral. Since bulbar nerves (like the motor trigeminus, accessory, hypoglossus, and upper branch of the facial) are affected, the clinical picture will closely simulate the paralyses originating in the nuclear regions of the oblongata and the pons. The symptoms of this combination of hemiplegias are, therefore, spoken of as *pseudobulbar symptoms*. Pseudobulbar symptoms may be occasioned either by two hemispheric lesions coming on simultaneously, or by the addition of a fresh lesion of one hemisphere to an old hemiplegic lesion of the other side. The latter has destroyed the fibers of the hemisphere corresponding to the nerves in question, but for well-known reasons has caused no symptoms.

Similarly, in complete conformity with the theory of bilateral innervation, experience teaches that as soon as a hemiplegia of the other side is added to the first hemiplegia of patients who have retained but slight residual effects of such a hemiplegia, the side first affected promptly becomes more seriously paralyzed, because the compensatory influence of the other hemisphere now disappears.

III. CEREBRAL SENSORY DISTURBANCES

The sensory tract in the brain may be involved in a number of entirely different locations, as a clinical result of which there will be a more or less distinct unilateral disturbance of sensation. A portion of the cerebral sensory tract, however, is so fused that a circumscribed lesion producing marked sensory disturbances can be situated only in certain locations. These places are found exclusively in the compact portion of the sensory tract which is formed by the fillet. The sensory fibers of the fillet arise from the nucleus gracilis and nucleus cuneatus in the medulla, partly cross to the opposite side, in the so-called decussation of the fillet, run through the tegmentum of the crus cerebri to the ventral nucleus of the optic thalamus. From this point they are connected with the parietal lobe and the motor region by means of the thalamic radiations which pass through the posterior part of the posterior limb of the internal capsule.[1] (See Fig. 428.)

Hemianesthesia may consequently be observed as the result of lesions: in the posterior columns of the medulla; in the pons if the region of the fillet be affected; in the tegmentum of the crus, when the lesion is situated between the red nucleus and the substantia nigra; in the subthalamic region and the adjacent posterior portion of the internal capsule (see Fig. 428); in the fibers of the corona radiata proceeding from the optic thalamus; and in extensive lesions of the parietal lobe, particularly when they involve the inferior parietal lobule, and of the central convolutions.

Cerebral hemianesthesia is most frequently dependent upon a lesion in the posterior portion of the internal capsule. Milder degrees of sensory disturbances may originate in the most varied locations in the brain, dependent upon the diffusion of that portion of the sensory tract which is not contained in the fillet, but very little is known about them.

The Character of Cerebral Hemianesthesia Produced by Anatomic Lesions, and Its Differentiation from Hysteric Hemianesthesia and Spinal Hemianesthesia. –The cerebral hemianesthesia due to anatomic causes is characterized by the fact that it involves the spinal sensory tracts, together with the cutaneous area supplied by the trifacial; in some cases the optic tract may also be involved, and, in rare instances, the acoustic tract. Involvement of the optic tract occurs when the lesion affects the sensory fibers in the region of the posterior portion of the internal capsule, or those in the corona radiata of the optic thalamus, when it involves the optic radiation (see Fig. 428, p. 1099), passing near the subthalamic region from the primary optic centers, *i. e.*, the pulvinar and external geniculate body to the cerebral cortex, or when it implicates the primary optic centers themselves. The

[1] The cerebral course of the sensory fibers from the anterolateral columns of the cord (see Fig. 455, and Fig. 456, p. 1142), which in physiologic and pathologic importance are second only to those of the posterior columns, is as yet unknown. Clinical experience would lead us to suppose that at least some of these fibers become associated with those of the fillet.

acoustic tract is affected when the lesion involves the internal geniculate body and posterior corpus quadrigeminum, or the acoustic radiations (see Fig. 428, p. 1099), which connect these structures with the temporal lobe. Visual disturbances in cerebral hemianesthesia dependent upon anatomic causes are always hemiopic in character, since the visual center is cut off from the retinal halves corresponding to the side of the lesion. Hearing is simply impaired and never abolished upon the side opposite to the lesion, since each acoustic nerve is connected with both temporal lobes. (See diagram, Fig. 403, p. 1041). Smell and taste are always retained, because the lesion is at some distance from the olfactory and gustatory fibers These fibers from each side are connected with both hemispheres and do not run in a compact bundle, so that they cannot easily be destroyed by a circumscribed lesion Cerebral hemianesthesia is further characterized by the fact that all the sensory powers may be involved—touch, pressure, pain, temperature, bone-sensation, the perception of the position and of passive motions of the extremities, and stereognostic sense, although they are usually very incompletely affected. The perception of the position and of passive motions of the extremities and the stereognostic recognition of objects are most affected and may be completely abolished, while the sensations of touch, pain, and temperature are usually simply diminished. The disturbance is most marked at the distal ends of the extremities, possibly because this region is supplied by a comparatively larger number of crossed fibers from the opposite hemisphere, while the proximal portions of the extremities are presumably supplied by fibers from both hemispheres. If the cause of the hemianesthesia be situated in the pons or in the uppermost portion of the medulla, a so-called alternating hemianesthesia may be produced, since the sensory trigeminus is involved below its decussation and is paralyzed upon the side opposite to the anesthetic extremities. The hemianesthesia frequently extends somewhat beyond the median line of the body, because the cutaneous terminations of the peripheral sensory fibers overlap the median line.

Since the cerebral hemianesthesia is crossed, *i. e.*, situated upon the side opposite to the lesion, it must be assumed that the sensations for one-half of the body are received, for the most part, by the opposite half of the brain. Since a triple decussation is improbable, we are led to suppose that the cerebral decussation (occurring chiefly in the decussation of the fillet) involves only those fibers which do not decussate at lower levels. (See Fig. 448.) This fact explains why the complicated conditions of spinal hemianesthesia (see p. 1125 et seq.) are absent in hemianesthesia of a cerebral type.

Hysteric hemianesthesia differs from anatomic cerebral hemianesthesia in the fact that, together with the different qualities of sensibility of the skin and more deeply situated organs (at times even the bones), including the distribution of the trigeminus, the higher senses are usually involved, not only sight and hearing, as may be the case with a cerebral lesion, but also smell and taste. The visual disturbance is amblyopic rather than hemiopic, and consists of diminished sharpness of vision, together with narrowing and pathologic fatigue weakness of the visual field upon the hemianesthetic side. The auditory phenomena may consist of a complete unilateral deafness, which does not occur in anatomic cerebral hemianesthesia. It must, nevertheless, be noted that the higher senses may not be involved in hysteric hemianesthesia. It is rather characteristic of this form of hemianesthesia that the most markedly disturbed sensation is that of pain. In regard to the variations in the sense of muscular contraction in hysteric disturbances of sensation and those of anatomic origin, see p. 952.

Sensory Disturbances with Cortical Lesions.—Sensory disturbances with cortical lesions require particular consideration, since there is a conflict of views in reference to this subject. As the sensory terminals extend over a very large cortical area and are more diffused than the terminals of the motor tract, it is apparent that a localized cortical lesion can produce only a partial disturbance of sensation. These sensory disturbances are most marked in lesions situated in the so-called motor region and in lesions of the parietal lobes. These areas receive the termination of the thalamic rediation which conducts the fibers of the fillet to the cortex. It is likely that sensory fibers of different qualities terminate heterogeneously in both these areas, and that the location and extent of the pathologic lesion is indicated by the degree rather than by the nature of the sensory disturbance. The character of the sensory disturbances in lesions of the so-called motor area has a special practical interest, since such disturbances play an important, though still somewhat uncertain, rôle in the localization of these lesions. In the first place, it should be noted that sensory disturbances are not constantly observed with lesions of the motor area. From what has previously been said, we are led to

suppose that they are absent when the lesion is quite circumscribed. In extensive lesions of the motor area, however, the motor symptoms are usually accompanied by sensory disturbances. They are almost always most pronounced and sometimes present exclusively in the distal portions of the extremities, particularly in the terminal phalanges of the fingers. This peculiarity, which has been previously referred to as characteristic of cerebral hemianesthesia caused by a more deeply situated lesion (p. 1090), is probably due to the fact that the proximal portions of the extremities send sensory fibers to both hemispheres. It is well known that the analogous statement is true in reference to motor disturbances. (See p. 1088.) A further characteristic of cortical disturbances of sensation is that they affect those sensory functions which are dependent upon the correlation of sensory impulses, rather than the individual qualities of sensation themselves. The sensations for pain, touch, and temperature are usually but slightly if at all affected, while there are distinct disturbances of the stereognostic sense, of the perception of the position, and of the passive movements of the extremities, as well as impaired localization of the sensations of touch and pain.

This is perfectly clear in regard to the stereognostic sense and the perception of the position and passive movements of the extremities, because it is only after the individual sensations reach the cortex that they are elaborated as such. The same must also be true of the localization of sensations; for, although it is primarily dependent upon the individual conduction of sensory impressions, the realization of these sensations in the cortex for localization purposes is a complicated function of deduction, which is accomplished through the association pathways. Confirmation of this is obtained by the clinical observation that localization of sensations may be destroyed, although its elementary sensations themselves are fairly well preserved.

IV. VERTIGO

Vertigo is a peculiar pathologic phenomenon which plays a great rôle in neuropathology, and is characterized clinically by a feeling of uncertainty as to the position of the body in space. With this there is physiologically associated the discomfort attendant upon disturbed equilibrium; in severe cases there are also motor disturbances of equilibrium. Other physiologic sequelæ of vertigo are the apparent movement of objects,[1] due chiefly to disturbance of visual perceptions (*rotary vertigo*) and affections of other sensory perceptions, particularly of the sensation of contact between the soles of the feet and the floor (apparent undulation of the floor). More remote sequelæ, produced by reflex action, are nausea and vomiting, a sense of faintness, palpitation, and even loss of consciousness.

The Pathogenesis and Clinical Significance of Vertigo.—The origin of vertigo, in many instances, is to be sought in the function of the semicircular canals of the labyrinth. At the present time it may be regarded as established that the function of these structures is to acquaint the individual with the position of his body in space. The sensory tract involved is the vestibular nerve, which innervates the semicircular canals; the other nerves of spinal sense are not involved in this function. The perception, the maintenance, and sense of equilibrium are simply special instances in which this function is employed, and the author does not believe we are justified in regarding the semicircular canals as the mechanism of a special "sense of equilibrium" or of a "static sense." It would seem more correct to designate them as an apparatus for the perception of space. It is equally erroneous to speak of the cerebellum as the organ of equilibrium, simply because it is the first central station for the impulses coming from the semicircular canals. Equilibration is but one of a number of functions of the cerebellum. The cerebellum serves rather for general orientation in space and for the adaptation of motor innervation to the position of the body; as the first central station, it receives and conducts to higher levels the impulses from the vestibular nerve, and from the direct cerebellar and Gower's tracts. The peculiar and wonderful arrangement of the mechanism for the perception of space need not be discussed in detail; it is enough simply to point out that the three semicircular canals are arranged in the three planes of space and surely are concerned with orientation, since every movement of the body (*i. e.*, of the labyrinth) is analyzed into its three components, each of which exerts an exciting influence upon the nervous elements of one of the semicircular canals. The exciting influence is doubtless due chiefly to the displacement of the endolymph upon the walls of the labyrinth which occurs with every move-

[1] As we shall subsequently learn (p. 1093 et seq.), this may also be the cause of the vertigo.

ment as a result of its inertia. But since we are conscious of our position even during rest, it must be assumed that static pressure effects may also act as the exciting influence which serves as a basis for the perception of space. The nervous impulses arising in this manner are first conducted to the cerebellum by that portion of the auditory nerve called the vestibular nerve. The apparent double function of the auditory nerve seems to justify Ewald's suggestion that it be named the nervous octavus; we should not elevate the vestibular nerve to the rank of a special cranial nerve, for the reason that the current terminology of these nerves is too firmly fixed in our literature. The nervous impulses received by the cerebellum are possibly metamorphosed and then conducted to the cerebrum.

From these physiologic facts it will be understood that a sensation of vertigo always arises when there is a contradiction between the nervous impulses from the semicircular canals and the position of the body (*i. e.*, the labyrinth) or the indication of the other sense organs. This contradiction causes the symptoms of vertigo — uncertainty of judgment, together with the resulting consequences for the motor innervation of the body, particularly for the maintenance of equilibrium, concomitant discomforts, and the characteristic secondary reflexes. In this manner the majority of the clinical symptoms of vertigo are easily explainable.

Vertigo occurs particularly in *affections of the labyrinth* which paralyze or irritate the end-organs in the semicircular canals, and thus lead to a pathologic distribution of the exciting influence and to a consequent faulty perception in reference to the position of the body. The classic example is Ménière's disease, in which the violent pathologic excitation of the semicircular canals produces such marked vertigo that the patient cannot maintain the erect position. In some of these cases the sensory perception of space may be suddenly and completely abolished, and this may result in an interruption of some of the association-fibers, so that unconsciousness is produced. The vertigo which is observed with innocent middle-ear affections is also to be referred to an associated involvement of the labyrinth, either in the form of circulatory disturbances or of variations in the intralabyrinthine pressure. All these cases are characterized as otogenic on account of the simultaneous disturbances of the acoustic function of the auditory nerve, disturbances which take the form of either impaired hearing or the presence of subjective auditory sounds. In these cases conditions either of excitation or paralysis within the semicircular canals may produce the phenomena of vertigo if all the semicircular canals be not equally affected.

The symptoms of vertigo so characteristic of *cerebellar disease* are evidently due to the fact that the stimuli for the sensory perception of space are correctly originated in the labyrinth, but not properly conducted, becoming blocked in the cerebellum. The so-called cerebellar ataxia, so frequently observed associated with vertigo in cerebellar disease, is made up of two components. One of these has nothing whatever to do with the sensory perception of space, but is associated with that disturbance of muscle tone which Luciani has demonstrated in cerebellar lesions. The other component is to be regarded as the motor effect of the vertigo, *i. e.*, the result of the defective correction of movements on account of faulty perceptions of space. (See p. 965.) Since the sensory perceptions of space are prepared in the cerebellum, but do not become conscious sensations and concepts until they reach the cerebrum, it will readily be understood that affections of the cerebrum, as well as those of the cerebellum, may lead to vertigo. The frequent and marked clinical similarity between tumors of the frontal lobe and those of the cerebellum indicates that the frontal lobe contains centers which receive the sensory perceptions of space by means of fibers radiating from the cerebellum and passing through the superior cerebellar peduncles and red nucleus.

The vertigo which occurs as a functional symptom of *circulatory disturbances, cardiac diseases, arteriosclerosis, anemia*, etc., is possibly due to abnormal excitability or abnormal excitation of the semicircular canals or of their coördinated centers. The same applies to *neurasthenic vertigo*.

The vertigo associated with *paralysis of the ocular muscles* is evidently due to a false projection of the retinal images, as a result of which disturbances of space-orientation might naturally give rise to vertigo. These disturbances of space-orientation are due not only to the occurrence of double images, but also to the fact that these retinal images become abnormally displaced during ocular movement, *i. e.*, they do not conform with the motor impulses, so that the objects apparently seem to move. In unilateral ocular paralysis the vertigo may be controlled to a variable degree by having the patient concentrate his attention upon the image produced in the sound eye, and disregard the faulty projection of the image in the paralyzed organ. Even in bilateral paralysis of the ocular muscles the vertigo may

be eliminated if the patient can learn to disregard the visual sense in the formation of his conceptions of space. In all cases the vertigo produced by paralysis of the ocular muscles may be made to disappear by closing either one or both eyes.

A special variety of vertigo, partly also of ocular origin, is that which is experienced upon *rapid rotation of the body* or upon the sudden arrest of a passive movement involving the body, such as the stopping of a train. In the first instance the phenomenon is probably dependent upon the fact that a physiologic excitation is produced in the semicircular canals by the motion imparted to the body, which results in reflex stimuli to the ocular muscles, so that the eyes unconsciously follow external objects in spite of the movement of the body. [Physiologic nystagmus.—Ed.] When the particular rotation is very rapid, the excitation of the semicircular canals becomes so strong (all the more as the stimulus increases in the same direction) that the reflex stimulation of the ocular muscles is excessive; since these ocular movements are unconsciously executed, the objects themselves apparently move and vertigo is consequently produced. The inability to fix the eyes permanently upon any object, together with the violence and rapid change in the excitation of the individual semicircular canals, may also be a factor in producing the disturbance of space-orientation in this variety of vertigo. The vertigo which is experienced by many individuals upon the sudden stopping of a train is probably due to the fact that the unconscious reflex ocular movements, produced through the agency of the semicircular canals, are continued somewhat longer than the motion of the train, and the apparent motion of external objects results in vertigo as before.

Mountain vertigo, or the vertigo of elevation, is not a pure vertigo, but is partly due to a sensation of fear. The other factor is probably an ocular vertigo dependent upon a strong concept of falling, which, by autosuggestion, innervates the nervous mechanism of space-orientation to an abnormal degree.

Agoraphobia.—Vertigo produced by the fear of space is brought about by an analogous mechanism which is excited by autosuggestion.

Sea-sickness is probably nothing else than a violent vertigo with numerous irradiations (to the vomiting center, etc.), produced by pathologic excitation of the semicircular canals as a result of the rolling and pitching of the ship. Ocular vertigo plays an important rôle in sea-sickness and originates in the labyrinth, just as is the case in the vertigo produced by rapid rotation of the body or upon the sudden stopping of a train. This is borne out by the fact that a large number of the phenomena of sea-sickness disappear when the eyes are closed. Since the symptoms by no means completely disappear, however, it is quite likely that a further cause is to be found in the inability of the mind and the movements of equilibration to follow the rapidly changing and violent excitations of the semicircular canals. The vertigo in sea-sickness is especially severe because the exciting impulses are constantly undergoing violent variation in a way that cannot be anticipated, and the result is, therefore, a real disease.

Galvanic vertigo, produced by the application of a galvanic current to the head, is doubtless dependent upon a direct and unequal excitation of the nerve-terminals of the semicircular canals, which does not correspond with the position of the body.

The existence of the so-called *gastric vertigo* of Trousseau (vertigo e stomacho laeso) in affections of the stomach is doubtful. The majority of the cases answering to Trousseau's description have been shown to be other varieties of vertigo (particularly aural vertigo), the origin of which was unknown in the life-time of this distinguished clinician. In many such cases the only symptom suggestive of gastric disease is the vomiting produced by the vertigo.

V. CEREBRAL LOCALIZATION

Without intending to enter into the question of cerebral localization, which belongs more properly to the province of special diagnosis, the author wishes to submit the following diagrams, to be utilized as a sort of guide in the problems of cortical and nuclear diagnosis:

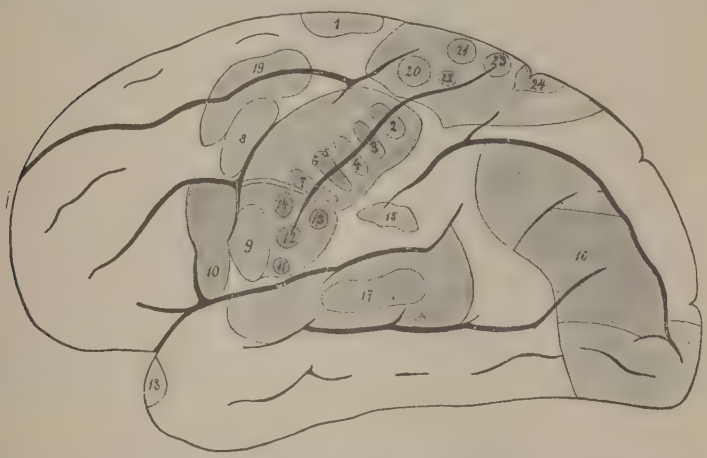


Fig. 424.—Cortical localization: 1, Trunk; 2, shoulder; 3, elbow; 4, wrist-joint; 5, the three last fingers; 6, index-fingers; 7, thumb; 8, "writing center" (assumed by French writers) (see p. 1107); 9, larynx; 10, Broca's speech center (motor); 11, tongue; 12, mouth; 13, lower facial; 14, upper facial; 15, eye muscle; 16, vision; 17, hearing (Wernicke's sensory speech center); 18, taste; 19, conjugate movements of eyes and head; 20, movements of hip-joint; 21, movements of knee-joint; 22, movements of ankle-joint; 23, movements of great toe; 24, movements of little toes (from Debove and Achard).

See p. 1046 in regard to the central innervation of the conjugate movements of the eyes. Wernicke has assumed that the center for these movements is situated in the inferior parietal convolution, because he found but few projection fibers in this region. He supposes (just as in the explanation on p. 1046) that the conjugate deviation of the eyes, which arises in case of lesions in this area, is due to lesion of an association tract, demonstrated by himself to exist between the visual area and the motor area.

Flechsig disputes this. He locates the "visual center" almost exclusively in the median surface of the hemispheres, especially in the region of the calcarine fissure. The visual disturbances so frequently met with clinically in lesions of this region (16) may be explained partly by the fact that such lesions often involve the visual fibers situated more deeply and connecting the central fibers of the optic tract to the visual center. (See Fig. 443, p. 1116.)

Flechsig[1] places the center of hearing in man (*i. e.*, the central terminations of the acoustic fibers) principally in the anterior transverse parietal convolution which is concealed in the Sylvian fossa and in the contiguous part of the first temporal convolution.

According to Flechsig, the center or area for smell in man has allotment both in the frontal and temporal portion of the brain. The former embraces the entire posterior portion of the base of the frontal lobes and the basal portions of the gyrus fornicatus; the latter embraces the uncinate gyrus and a part of the adjoining inner pole of the temporal lobe. Both portions are fundamentally connected with the island of Reil.

Flechsig, who has recently investigated the localization of the sense of taste, does not furnish any definite statements about its seat; 18 in the diagram is, therefore, placed provisionally.

Munk locates the region for somatic sensibility in that part of the central convolutions and the paracentral lobule supplied with motor centers. (See Flechsig, Gehirn und Seele, Leipsic, Veit & Co., 1896.) That is to say, these areas contain, in addition to the motor centers, the central apparatus for sensory appreciations in so far as they do not belong to the "higher" senses (sight, hearing, etc.), which possess special centers. The area for corporeal feeling, according to Flechsig, also includes the lobus limbicus, *i. e.*, the gyrus fornicatus, gyrus uncinatus, and the gyrus hippocampus.

The unshaded areas and the shaded area of the parieto-occipital brain, 16, according to Flechsig, wrongly credited with the visual center, contain the Flechsig association centers. He differentiates three, viz., the frontal or anterior, the parieto-occipitotemporal or posterior great association center, and finally the Island of Reil. These areas are anatomically characterized by containing no projection fibers, or very few, and, on the contrary, very many association fibers. Lesions of the anterior association center should cause a loss of interest and a change of character; lesions of the posterior association center, a loss of collective representations, positive knowledge, and mental capacity.

[1] Neurolog. Centralbl., 1908, No. 1, p. 2.

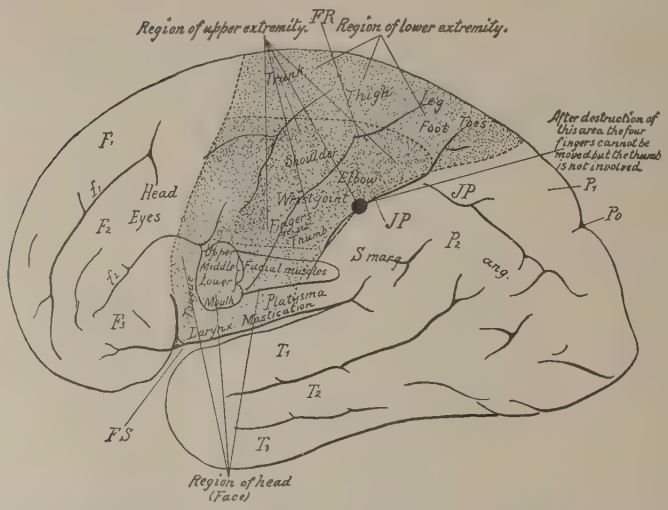


Fig. 425.—The lateral aspect of the human cerebral hemisphere. The motor areas, according to Allen Starr, Keen, Chr. Mills, Horsley, and v. Monakow, as arranged by the latter.

Fig. 426.—The motor areas in the ape (Macacus sinicus), according to Beevor and Horsley.[1]

(See Figs. 427 and 428, p. 1097, for the following legends.)

Fig. 427.—Horizontal section representing the motor points of irritation of the internal capsule of the ape, according to Beevor and Horsley: *FS*, Fissura Sylvii; *Li*, lenticular nucleus; *Th.* optic thalamus; *ant. ci*, anterior limb of the internal capsule; 1, movement of the eyes to the contralateral side; 2, movement of the eyes to the same side; 3, movement of the mouth to the opposite side; 4, movement of the head to the same side; 5, movement of the tongue; 6, retraction of the mouth; 7, shoulder; 8, elbow; 9, wrist; 10, fingers; 11, thumb; 12, trunk; 13, thigh; 14, tarsus; 15, knee; 16, great toe; 17, toes.

Fig. 428.—Schematic horizontal section through the internal capsule, with the positions of the most important tracts.

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[1] In regard to the relations in the anthropoid apes (orang-utang) see Beevor and Horsley, Phil. Trans., 1890, B., Pl. 21.

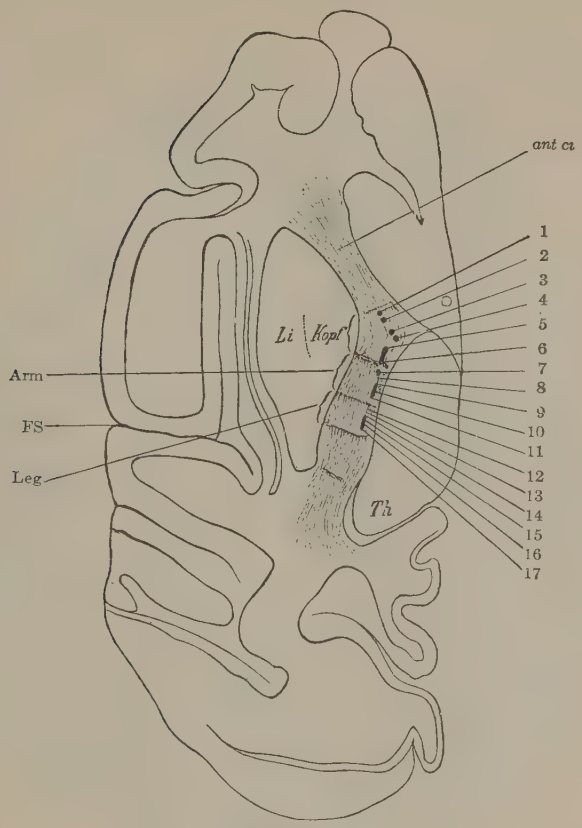


Fig. 427.

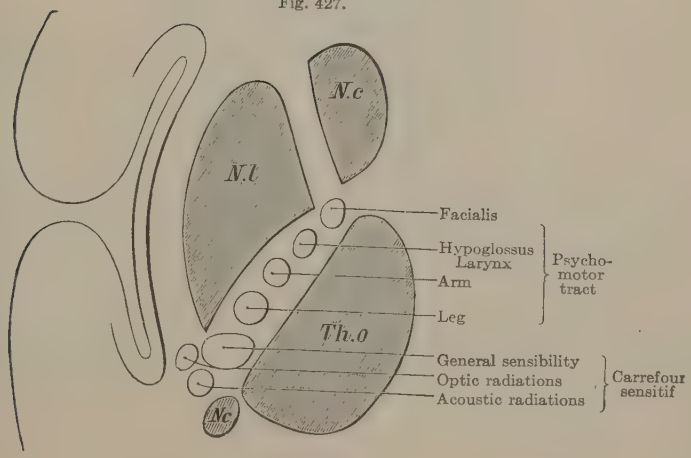


Fig. 428.

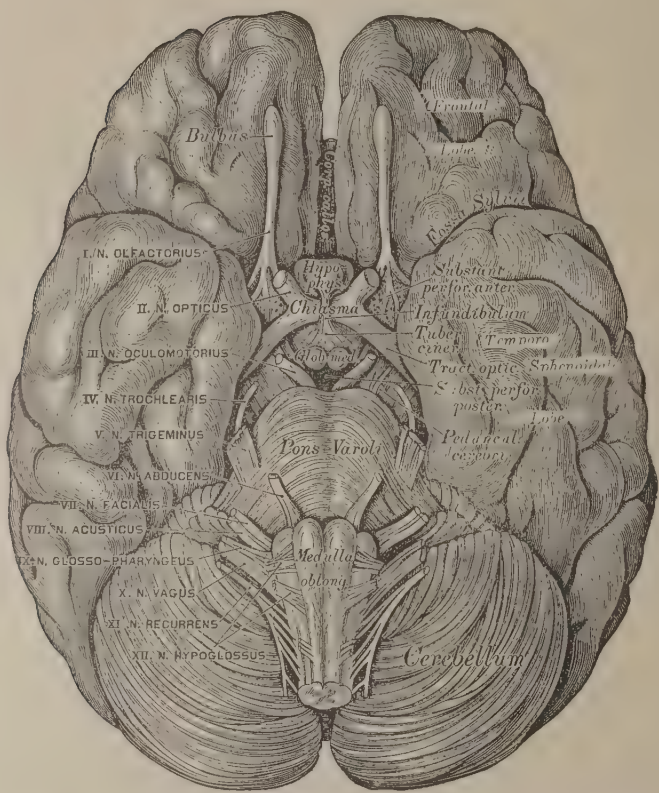


Fig. 429.—Base of the brain, showing the origin of the cranial nerves (from Heitzmann).

(See Figs. 430 and 431, p. 1099, for the following legends.)

Fig. 430.—Transparent surface view of the medulla oblongata from behind. Upon the right side the nerve nuclei are put in diagrammatically and numbered with small Roman figures; *V*, Motor nucleus of the trigeminus; *V′* and *V″*, middle and lower sensory nuclei of the trigeminus; *VI*, abducens nucleus; *VII*, facial nucleus; *VIII*, posterior median acoustic nucleus; *VIII′*, anterior median acoustic nucleus; *VIII″*, anterior lateral acoustic nucleus; *IX*, glossopharyngeal nucleus; *X*, vagus nucleus; *XI*, accessory nucleus; *XII*, hypoglossal nucleus; 1, brachium pontis; 2, brachium conjunctivæ; 3, cerebellar peduncle; 4, eminentia teres; 5, striæ acousticæ; 6, ala cinerea. The large Roman numerals represent the corresponding nerve-roots (Erb).

Fig. 431.—Transparent lateral view of a section through the right half of the medulla oblongata. To show the relations of the most important nuclei. The nuclei situated nearest the surface of the section are shaded darker (diagrammatic): *Py*, Pyramidal tract; *Py.Kr*, decussation of pyramidal tract; *O*, olive; *O.s*, superior olive; *V*, motor nucleus of trigeminus; *V′*, middle sensory nucleus of trigeminus; *V″*, lower sensory nucleus of trigeminus; *VI*, nucleus of abducens; *G.f.*, knee of the facial; *VII*, facial nucleus; *VIII*, posterior middle acoustic nucleus; *IX*, glossopharyngeal nucleus; *X*, vagus nucleus; *XI*, accessory nucleus; *XII*, hypoglossal nucleus; *Kz*, nucleus gracilis; *RV*, trigeminus root; *RVI*, abducens root; *RVII*, facial root (Erb).

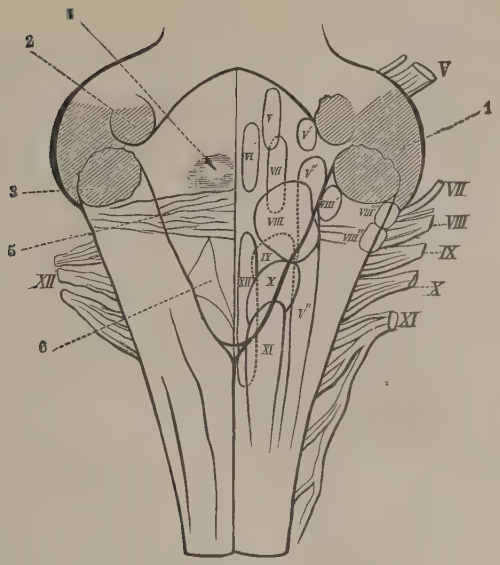


Fig. 430.

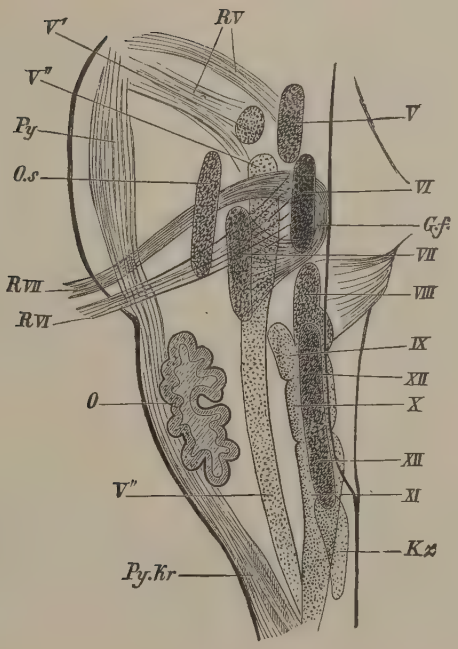


Fig. 431.

VI. THE DISTURBANCES OF SPEECH

INTRODUCTION

The following chapter on the disturbances of speech and the teachings on aphasia is founded chiefly on the epoch-making works of Wernicke and Lichtheim, but it includes other extensive studies, as well as the author's own investigations. In order to facilitaet the task of reference the most important literature on the subject is given below in alphabetic order, although no claims are made for its comprehensiveness.

Literature on Aphasia: Bastian, On Different Kinds of Aphasia, British Med. Journal, 1897. Broca, Sur le siège de la faculté du language articulé, Paris, 1861. Dejerine, Etude sur l'aphasie dans les lésions de l'insula de Reil, Revue med., 1885. Ibid., Différentes variétés de cécité verbale, Mém. de la société de biologie, 1892. Ibid., Contributions à l'étude anatomopathologique et clinique des différentes variétés de cécité verbale, ibidem, 1892. Dejerine and Ch. Miraillé, Sur l'alteration de la lecture mentale chez les aphasiques moteurs corticaux, Comptes rendus des séances de la société de biologie, Paris, 1895. Dejerine and Vialet, Contribution à l'étude de la localisation de la cécité verbale pure, communication faite à la société de biologie, 1893. Grashey, Ueber Aphasie und ihre Beziehungen zur Wahrnemung, Arch. f. Psychiatrie, vol. xvi. Kussmaul, Die Störungen der Sprache, Leipzig, 1877. Lichtheim, Ueber Aphasie, Deutsches Arch. f. klin. Med., 1884, vol. xxxvi. Naunyn, Ueber die Localisation der Gehirnkrankheiten, Congr. f. inn. Medicin, 1887. Oppenheim, Ueber das Verhalten der musikalischen Ausdrucksbewegungen und des musikalischen Verständnisses bei Aphasischen. Charité Annalen, 1888. Pick, Beiträge zur Pathologie und pathologischen Anatomie des centralen Nervensystems, Berlin, 1898. Sachs, Vorträge über den Bau und die Tätigkeit des Grosshirnes und die Lehre von der Aphasie und Seelenblindheit, Breslau, 1893. Wernicke, Lehrbuch der Gehirnkrankheiten, 1880. Ibid., Herderkrankungen des Unterscheitelläppchens, Arch. f. Psychiatrie, vol. xx. Ibid., Gesammelte Aufsätze zur Pathologie des Nervensystems, Berlin, 1893. Wernicke and C. Friedländer, Taubheit in folge doppelseitiger Läson des Schläfenlappens, Fortschritte der Medicin, 1883.

1. THE CONCEPTION OF THE MOTOR SPEECH TRACT

Speech arises from the elaboration of motor speech conceptions in the so-called motor speech center situated in the left hemisphere. When the will is exerted, these conceptions are responsible for the coördinated impulses proceeding through the so-called central speech tract to the bilateral cortical centers for the muscles of speech, thus generating the spoken word.

The speech tract (Fig. 432) originates in the motor speech center, the so-called Broca's area (*a*, Fig. 432), runs to the cortical centers for the oral, laryngeal, and respiratory muscles, some of the fibers possibly passing through the corpus callosum, and finally enters the pyramidal tract to reach the nuclei for the muscles of speech. From the cortical centers to the nuclei of these muscles the impulses travel through the same fibers that are utilized for the other functions of the muscles, so that an actual tract does not exist after the impulse leaves the cortical centers. The earlier assumption of a bundle of fibers belonging to the great psychomotor pathway, which ran directly downward from the center of motor speech to the speech nuclei is invalidated by the fact that motor aphasias are caused by lesions of the region about the center for motor speech only. Lesions in the centrum semiovale, in the crura, or in the pons and medulla produce, at the most, the clinical picture of anarthria, but not that of aphasia.

2. THE DISTURBANCES OF SPEECH FROM LESIONS OF THE SPEECH AREA OR OF THE CONDUCTING FIBERS

The innervation for the movements of speech may be interrupted by a lesion situated in any portion of its course. The clinical picture is subject to great variation, according to whether the lesion affects the speech center, the actual speech tract (the heavy line in Fig. 348), or simply the connection of the cortical centers of the muscles of speech with the nuclei of the latter (the light lines in Fig. 348). In the first instance, even though the lesion be circumscribed, the ability to form words will be more or less completely abolished. When the lesion affects the connection between the cortex and the nuclei of the muscles, however, the only result is a mutilation of the syllables and a disturbance of pronunciation; if the lesion be of moderate extent, the disturbance is but slight, since, owing to the commissural fibers,

the speech impulse is conducted downward from both hemispheres. As a result of the bilateral quality of this portion of speech innervation, the disturbance of pronunciation can be extreme only when the lesion is situated low down in the vicinity of the nuclei for the muscles, where the fibers of both hemispheres are simultaneously more or less involved.

The disturbances having as their cause some lesion in the speech center of the cortex or in the actual speech tract of the left hemisphere are called aphasias; those due to some lesion between the cortex and the nuclei for the muscles of speech are called anarthrias.

Although in typical cases the clinical distinction between these two conditions is quite marked, the differentiation between them is not sharp, since lesions of the speech center and of the actual speech tract may give rise to symptoms resembling anarthria, providing that the lesion is neither large nor destructive (see Anarthria). Such a disturbance, which might be called a "central anarthria," may, nevertheless, be differentiated from a peripheral anarthria, and particularly from that caused by a lesion in the vicinity of the nuclei, by the fact that in the latter the other functions of the muscles of speech (deglutition, mastication) are also involved.

The sharpest differentiation between aphasia and anarthria consequently consists of the fact that the former is purely and exclusively a disturbance of speech, while the latter is always accompanied by a disturbance of the other functions of the muscles of speech.

(a) Anarthria

In anarthria there is an affection of individual fibers of the speech tract in the neighborhood of the nuclei. Hence the following peculiarity: The speech im-

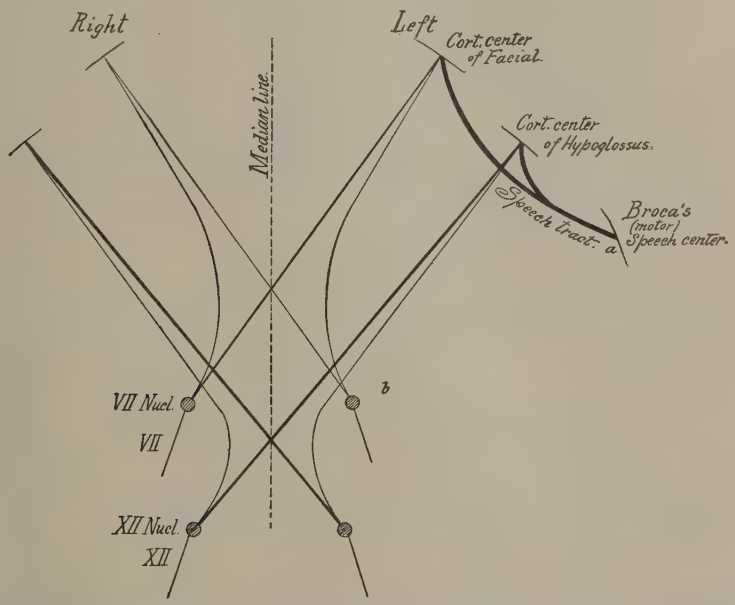


Fig. 432.—Diagram of the motor speech tract. For simplicity, of the nerves which subserve the function of speech, only the facial (*VII*) and hypoglossal (*XII*) are shown. For the center for voluntary breathing, as well as that for the larynx, see Fig. 425; and for the motor trigeminus, especially for the part that presides over the movement of the jaws, see "Chewing," Fig. 425. The figure also fails to picture the commissural fibers coursing in the corpus callosum, which unite the two lateral cortical centers.

pulse is correctly formed in the speech area and correctly despatched to the periphery; but, as the result of partial interruption of conduction in the neighborhood of the

nuclei, its ganglion-cells no longer receive the measure of innervation essential to coördinated speech. The result is a disturbance in the coördination of speech, analogous to the ataxia of the extremities in partial paralyses (see p. 964 et seq.), so that a patient with anarthria pronounces the word with approximately correct cadence of syllables and intonation, but with some of the letters of the word lacking or else incorrectly pronounced. Anarthria is, therefore, a disturbance of pronunciation, which is characterized by the fact that the more or less marked paralysis of the muscles of speech also affects the other functions of these muscles.

It is evident that quite an analogous disturbance of speech will arise when not the terminal fibers of the speech tract in the neighborhood of the nuclei, but the nuclei themselves or the peripheral speech nerves (*e. g.*, facial and hypoglossal) are affected. In such cases speech will be mutilated and pronunciation will suffer. These nuclear and altogether peripheral disturbances of speech parallel those of supranuclear anarthria, insomuch as they are associated with paralyses of other movements.

The clinical picture of anarthria may, under some circumstances, result even from an incomplete involvement of the speech center or of the actual speech tract. This can be explained only by assuming that the separate fibers or cells are to a certain extent individually diseased, or that the disturbance is purely functional without gross anatomic changes, because the fibers of the central speech tract are so compact that larger lesions generally affect them in toto. Anatomic proof of the existence of pure anarthria depending upon such individual disease of separate fibers or cells has not yet been furnished. Anarthric disturbances of pronunciation, which often persist for a long time after recovery from aphasia, or accompany incomplete aphasias, may without doubt be explained by the fact that certain individual fibers or cells of the central speech apparatus, which is at first widely involved, later on recover, while certain others do not. In the same way manifold combinations of anarthria and aphasia, which have been sometimes observed in incomplete aphasia, may perhaps be attributed to an unequal involvement of the central speech apparatus. As has previously been stated, the characteristic of all these cases of "central anarthria" is that the muscles perform all their movements except those necessary for the production of speech.

The simplest method of examining for anarthria is to have the patients pronounce the letters of the alphabet in their order, and then combinations of letters, *i. e.*, simpler and then more complicated words. Theoretically, it is evident that anarthria will occur very frequently in all lesions in the neighborhood of the nuclei of the speech muscles, *i. e.*, in hemorrhagic and softened areas and in tumors of the pons and of the oblongata, but especially in progressive bulbar paralysis.

(*b*) Aphasia (Agraphia; Alexia)

Mechanism of Interior Language

As contrasted with anarthria, we may define aphasia as embracing those disturbances of speech which arise from more or less complete interference of the func-

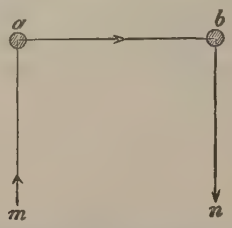


Fig. 433.—Primitive speech apparatus of the child for mechanical repetition of words: *a*, Sensory speech center (Wernicke's convolution); *b*, motor speech center (Broca's convolution); *bn*, motor speech tract; *ma*, acoustic tract (concerning those anatomic conceptions, see p. 1110). (For the anatomic relations, see Fig. 435.)

tion of the actual speech tract or of the motor speech center itself. If we could represent the latter as a mere center, the process would be comparatively simple; the arrest of function, both of the center (Fig. 432, *a*) and of the tract (heavy line, Fig. 432), would cause loss of speech or aphasia.

The conditions of aphasia are, however, more complicated, because the speech center is, in a broader sense of the word, not a simple motor center. We may consider the entire apparatus of central speech formation, which has been established psychophysiologically by the researches of Wernicke and Lichtheim, as proceeding centrally from the point *a* of Fig. 432, and this latter point as representing merely the motor terminus of the central speech mechanism, the so-called motor center of speech. Lesions of these portions of the speech apparatus, which have not yet been studied, can also give rise to disturbances properly designated as *aphasias*. To understand these different forms of aphasia, a knowledge of the physiologic mechanism of central speech formation is, therefore, required. A more exhaustive discussion, essentially following Wernicke and Lichtheim, must now be given.

When a child learns to speak, the sound of the word heard is sent by way of the acoustic nerve to the cortex of the left first temporal convolution (sensory speech center, Figs. 433 and 435). The child then attempts to imitate this word. This latter procedure may be explained by assuming that, by means of association, the auditory images beget a conception of movement corresponding to the spoken words. This representation of movement, as Broca proved, is situated in the left inferior frontal convolution (motor or Broca's speech center, Fig. 424, 10). The

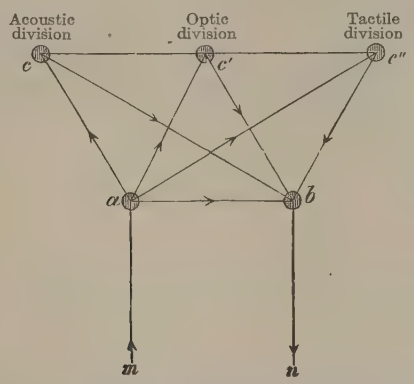


Fig. 434.—Apparatus for conscious speech and speech comprehension, with the relationship to the primitive speech center to concepts, especially the sensory division of the latter. For simplicity, merely three divisions of the cortical sensory areas have been represented. The letters *a*, *b*, *x*, *m*, and *n* have the same meaning as in Fig. 433.

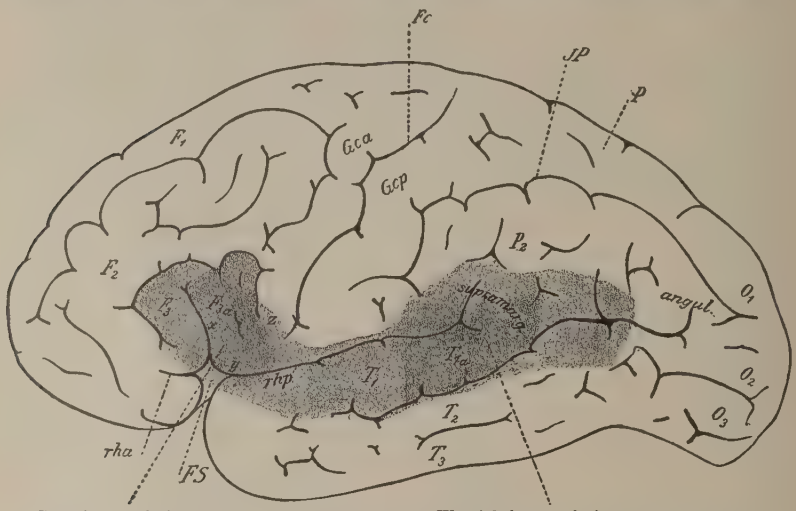
child's primitive speech apparatus (Fig. 433) is formed in this way, and he thus repeats mechanically the word spoken. *a* represents the center for auditory images of the word heard, *i. e.*, the *sensory speech center* in the first temporal convolution. The auditory images are received here after they have properly stimulated the corresponding acoustic center, the center of simple hearing or sound perception. The anatomic course of these tone images will be considered later on. (See p. 1110 et seq.) The association tract (*ab*) which, by mechanical babbling of the child, incites the center *b* by way of *mab*, runs, according to Wernicke, along the convolutions of the island of Reil from behind forward. The arrow pointing upward represents the tract of the auditory nerve (in so far as it concerns excitation of word images, see p. 1110); the arrow pointing downward from *b* represents the motor speech tract shown in detail in Fig. 432.

The child's advance to the stage of voluntary speech is attained through the association of centers (*a*) and (*b*) with concepts. The concept of an object is the aggregate of its partial representations. The concepts are acquired by experience, in that these partial representations are stored and associated as memories in the different sensory areas of the cortex.

The concept of an object can, therefore, never be localized at a single point in the cerebral cortex, *e. g.*, the concept "bell" requires association tracts to quite different parts of the brain to the acoustic, optic, and tactile centers. This is repre-

sented in the more complicated diagram (Fig. 434). The partial concepts $c + c' + c''$ first produce the concept bell.[1]

To simplify the speech scheme, we reduce the concept $c + c' + c''$ to a single point (C), using the diagram that Wernicke first made for voluntary conscious speech (Fig. 436). The significance of the double arrows will be explained in what follows. The diagram shows that voluntary speech follows the path *Cbn* (Fig. 436),



Broca's convolution Wernicke's convolution

Fig. 435.—The central areas of speech, according to von Monaków. Lateral view of the left hemisphere. Speech area shaded, the relative fields somewhat lighter: *FS.*, Fissure of Sylvius; *rha*, *rhp*, ramus horizontalis anterior and posterior, of the fissure of Sylvius; *Gca*, *Gcp*, anterior and posterior central convolutions; F_1, F_2, F_3, first, second, and third frontal convolutions; *Fc*, central fissure; *JP*, interparietal sulcus; O_1, O_2, O_3, first, second, and third occipital convolutions; T_1, T_2, T_3, first, second, and third temporal convolutions; *P*, superior parietal lobule; P_2, inferior parietal lobule; *supramarg.*, gyrus supramarginalis; *angul.*, gyrus angularis.

repetition (by avoiding its point C) follows the path *mabn* (to a certain extent just as do the reflexes), and the comprehension of spoken language follows the path *maC*.

The Aphasic Disturbances Without Reference to Written Language (Reading and Writing)

With the aid of this diagram we can readily explain many types of aphasia by supposing interruption of conduction at different places. We differentiate between motor and sensory aphasia according to whether the interruption affects the sensory centripetal (*maC*), or the motor centrifugal conducting portion (*Cbn*). Aphasia arising from interruption of conduction in the line *ab* is spoken of as "*conduction*" or, perhaps better, "*association aphasia*." Disturbances between *a* or *b*, on the one hand, and *C*, on the other, are called *transcortical*, those in *a* and *b cortical*, and those peripheral to *a* and *b* subcortical. These names have not been fittingly

[1] To avoid misunderstanding, the author should add that the concept which a child has of a bell and associates with the word "bell" is, of course, not the complete concept of a "bell" which an adult possesses. A complete concept will only be developed gradually, in the course of mental development, by adding one partial concept to another. Thus, in small children, the concept of a "bell" may be exclusively the partial representation of the tone of a "bell" and perhaps of some of its metallic luster; then, in the course of development, are superadded the concepts of the form of the "bell," of the sensation of cold by touching it, of its use, and of many other features to complete the concept.

chosen, since the entire area of innervation (*abc*) is situated in the cerebral cortex,[1] and should, consequently, be designated as cortical. If the terms had not become so fixed, the author would suggest replacing them by the expressions transcentral, central, and subcentral, the word "central" naturally referring to the speech center.

To explain these different symptom-complexes, we must now call attention to the fact that, for correct speaking, the tract *Cab* must be intact, as well as the tract *Cbn*, although this does not directly appear in the diagram. If the tract *Cab* be interrupted at any point, or the center *a* be destroyed, one might believe that only the sensory function of speech, *i. e.*, comprehension of speech and not its externalization, would be affected. Experience teaches us, however, that in this lesion speech is, as a matter of fact, possible by way of the tract *Cbn*, but that a symptom called *paraphasia*, *i. e.*, confusion of words (see below; the symptoms of central and transcentral sensory aphasia), is regularly observed, because the control of the motor innervation by way of the path *Cab* is essential for correct speaking. Since this paraphasia may also be caused by lesions between *C* and *a* (see below, transcentral sensory aphasia), it must be assumed that not only centripetal, but also centrifugal, conduction, requisite for the control mentioned above, is situated in the association fibers *aC*. Words are sounded inwardly. The double arrows in Fig. 436, between *a* and *C*, represent this idea; but it must be assumed that the innervation from *C* to *a* is not sufficient to speak by way of *Cabn*, as otherwise no loss of speech would occur with a lesion between *b* and *C*, and experience proves that this is not the case. The

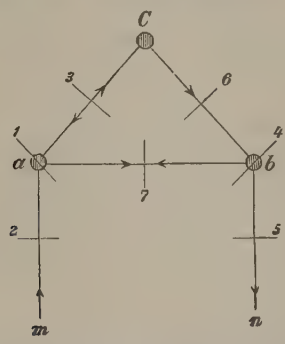


Fig. 436.—Simplification of the diagram of conscious speech (Fig. 434) by restriction of the conception to point *C* and the omission of the acoustic center *x*. The letters have the same meaning as in both preceding diagrams. The figures correspond to the list of aphasias in the text.

double arrow between *a* and *C* also indicates that, in addition to paraphasia, a disturbed naming capacity is peculiar to central and transcentral aphasia. This phenomenon, which is essentially closely related to paraphasia, consists in a difficulty to find the proper name for objects and ideas, because of a disturbed association between the concept and the auditory image. Paraphasia is developed from this whenever the patient, in his desire to talk, does not experience its inhibitory effect.

The following main types of aphasic disturbances should now be easily understood. The numbers represent the point of interruption as indicated in the diagram (Fig. 436):

1. *Central* (*Cortical*) *Sensory Aphasia*.—Comprehension of speech and repetition of speech are prevented. Paraphasia is present. Naming is disturbed. Objects are usually named wrongly.

2. *Subcentral* (*Subcortical*) *Sensory Aphasia* (Pure "Word-deafness").—The same functions are interfered with as in 1, except that there is no paraphasia, and no difficulty in naming. (See below, differences in regard to written speech.)

3. *Transcentral* (*Transcortical*) *Sensory Aphasia*.—Comprehension of speech is lost; repetition of speech (in contrast to 1) is retained. Paraphasia is present. Difficulty in naming is also characteristic. Objects are named wrongly.

[1] This is demonstrated by the fact that the lesions producing aphasia are always situated in the cortex or in its immediate vicinity. At most the tract *am* (the heavy line in Fig. 432) describes but a slight curve in the white matter in the vicinity of the cortex.

4. *Central (Cortical) Motor Aphasia* (Broca's Aphasia).—Spontaneous speech and capacity to repeat are lost. Comprehension of speech is preserved.

5. *Subcentral (Subcortical) Motor Aphasia* (Lesion of the Speech Tract; Pure Word Dumbness).—Clinical picture as in 4. Differentiation between 4 and 5 with regard to syllable counting and written speech is discussed below.

6. *Transcentral (Transcortical) Motor Aphasia.*—Spontaneous speech is lost. Repetition and comprehension of speech are preserved.

7. *Conduction or Association Aphasia.*—Comprehension of speech is preserved. Spontaneous speech is paraphasic. Repetition by way of *aCb* is possible, but also paraphasic. Naming is difficult. Positive cases of this kind of aphasia have not been observed. (See p. 1113.)

Difficulty in "naming" (see explanation, p. 1105) is common to the first and third form of sensory aphasia. With it, and with the necessity of using a limited stock of words, is associated agrammatismus, so frequently observed during the stage of recovery from sensory aphasia. It consists in a sort of telegraphic style, *i. e.*, of sentences without construction.

A type of syllable stuttering that cannot be distinguished from that of general paresis is very prominent during the subsidence of Broca's (central motor) aphasia, or in incomplete varieties of the latter.

A differentiation between 4 and 5 can be determined by examining the written speech. In central motor aphasia (4) writing is impossible; in subcentral (5) it is preserved. Further discussion of this point will be taken up later. Lichtheim has demonstrated that a patient with subcentral motor aphasia (5) can show by signs how many syllables there are in the name of an object held in front of him; whereas, with central motor aphasia (4), destruction of the center (*b*), this is impossible, although one might think that syllable counting could take place at the center for auditory images (*a*).

The varied disturbances of writing and reading which occur in aphasia show that the centers *a* and *b* have an almost reciprocal relation, expressed in Fig. 436 by the double arrows, and that the sensory and the motor concepts together produce the unit of so-called word conception (Wernicke) (see p. 1107). In this collective word conception, and not merely in the individual concepts (*a* and *b*), are to be found not only the letters, as we shall see, but also to a certain extent the number of the syllables, presupposing an internal speech. Therefore, in case there is an injury in *a* and *b* or between the two, the patient can no longer determine the number of syllables in a word corresponding to some conceived object. Thus far the author believes this phenomenon has been attributed only to lesions in *b*: that is, to central motor aphasia (4). However, if this explanation be correct, it must also occur in central sensory and in association aphasia.

The reasons why all aphasias have not been given among the forms described above will appear later on p. 1118.

Disturbances of Written Language Associated with Aphasia

In determining the characteristics of an aphasia, we must inquire into written speech, *i. e.*, the ability to write and to read, for this is closely connected with articulate speech. This gives the clinical pictures of the different forms of aphasia a much more sharply defined character, since the functions of written speech appear differently in these disturbances, according to the location of the lesion.

To explain the psychic mechanism of reading and writing, one cannot do better than to start again with the development of this function in children.

The child learns to read and write by having the optic pictures of the letters imprinted upon a center (α, Fig. 437) (the position will be indicated later); and by learning at the same time to associate with them the corresponding auditory images. This association results from the formation of a tract ($\alpha\ a$), in which *a*, as in Fig. 436, represents the sensory (acoustic) speech center. By means of such an association, printed or written letters acquire a definite significance to the child. In learning to write, a child forms an association between the optic center (α) and a motor center (β), and making use of β, learns to copy the letters mechanically. There first occurs an impression of sensory memory pictures (here by way of the optic), an almost simultaneous association of these with acoustic memory pictures, and then a production of movement concepts for writing the separate letters. Therefore, we assume that copying letters by a child occurs by way of the tract ($\mu\alpha\beta\nu$).

Thus far we have included in the child's learning written speech only the mechanical copying of letters. Very soon, however, he learns to write letters when merely their auditory images have impressed him, either from dictation or of his own accord,

representing on paper the letters resounding spontaneously in his mind. To explain the process of writing letters voluntarily or from dictation, we must introduce into our diagram still another centrifugal tract, which unites the diagram of writing with that of speaking. We have already in the tract $a\,a$ (Fig. 437) a centripetal connection of the writing mechanism with a sensory speech center; the line $b\mu$ may represent the centrifugal connection between the motor speech center (b) and the psychic writing mechanism. The mechanism of writing described above and personal observation show us that this connection occurs from b to a and not from b to β, since we always arouse the optic letter image first in writing and then produce it by means of our motions. Writing letters voluntarily or from dictation takes place, then, in this way: a is stimulated by the auditory images of the letter emerging from the mind, and excites in b the concept of movements of the spoken letter, then the optical picture in a, and from there finally the movement concept of the written letter in β.

The point β has oftentimes been supposed to exist as an actual writing center (Charcot, Exner, Pitres, Ziehen); and Exner located in it the second frontal convolu-

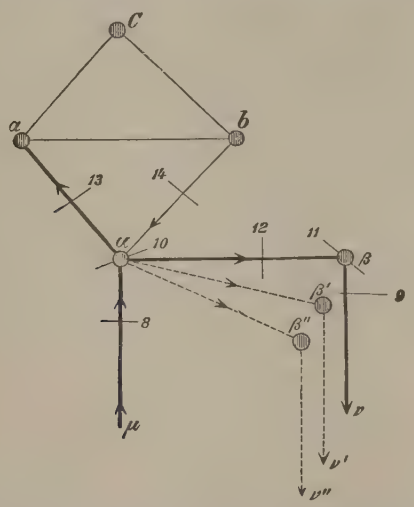


Fig. 437.—Diagram for the mechanism of written speech: a, Center for the optic concepts of written or printed letters apparently corresponding to the bilateral cortical optic center (p. 1115); μa, optic tract (see p. 1115); a, sensory speech center; b, motor speech center; C, concept; β, β', β'', motor centers for writing movements (β for writing with the right hand; β' and β'' for writing with other parts of the body); $\beta\nu$, $\beta'\nu'$, $\beta''\nu''$, motor tracts for writing movements. The numbers 8 to 14 represent the locations of lesions in the so-called isolated alexias and agraphias. (See p. 1113.) For simplicity only, the heavy lines should be noticed at first in reading the text.

tion on the left side, near the middle of the anterior central convolution. (See Fig. 1095, 8.) Simple reflection shows that such actual writing center does not exist. The movement of writing is, as a matter of fact, like any other movement, in case the form of the letter is known; one can write it with any part of the body, for example, the nose or the foot. We can go even so far as to place the supposed writing center in the brain of the horse when we describe the form of a letter by riding. As a matter of fact, we write by copying approximately the optical memory pictures of letters, using any sort of movements. Ordinarily, β represents the cortical center of the right hand; it could, however, just as well represent another motor center. The dotted tracts $a\beta'_1{}'$, $a\beta''_1{}''$, etc. (Fig. 437), are intended to express this multiplicity. Including only the essentials of Figs. 436 and 437, a diagram of the central speech mechanism, including reading and writing, may be represented as in Fig. 438.

The following explanation should be added to explain reading and writing entire words. Experience teaches that written speech is always disordered in aphasias if there be an injury anywhere upon the line ab, whether it be at a or at b, or between the two; for, as mentioned upon p. 1106, a and b seem like a unit, which Wernicke has designated as the "substratum of the word conception." Now, it

is ordinarily assumed that the word conception is produced from separate letters, that the tract *aab* is traveled by each letter, and that in writing entire words the conception will be dissected, so that an innervation impulse proceeds from *b* to *a* for each letter. It might be said against the theory of reading by spelling, and in favor of the theory that optic memory pictures of entire written words are stored up in the brain, that in the speed-reading of experts, not merely words, but sentences, and even whole pages, are glanced over in an interval apparently too short for the time required for the individual conduction of words. This objection is really not valid, however, because the curtailment of the procedure, through practice, depends upon the evocation of acoustic word-memory images, through the perception of characteristic letters or combinations of letters, and not upon the apperception of optic images of words, sentences, or whole pages as such. In this manner the sense of words is conjectured from the letters, sentences from characteristic word combinations, and pages from peculiar sentences. The ability to conjecture, *i. e.*, to supply the deficiencies in perception, plays a very important part in shortening the time of apperception of sensory impressions. In the same way, only a cursory glance at the unusual styles of print on the modern posters at every corner is necessary, although a direct recognition of these very unusual optic word images, seen perhaps for the first time, is manifestly inconceivable. The ability to decipher illegible handwriting might be adduced as further proof. In many of these instances it is hardly a question of real letters at all, and one might

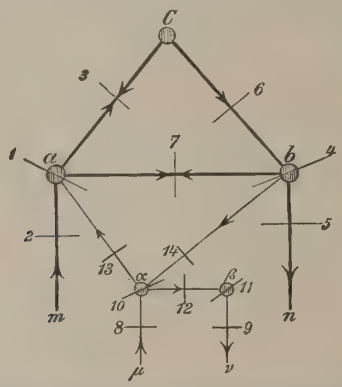


Fig. 438.—Diagram of the entire central speech apparatus, including reading and writing. The letters and the figures have the same meaning as in the two preceding illustrations.

think that entire word images are read. This is impossible, however, because the forms of these distorted, illegible word images vary so in each instance that they cannot be stored up in the brain as memory pictures. The mechanism consists rather in the recognition of individual letters, the characteristic grouping of which permits the conjecture of the rest, *i. e.*, the whole word. From the words, even if there be many undecipherable ones, we guess the sense of the sentence, as every one who has had experience can confirm.

Of course, this applies only to languages (European) which possess an alphabet. The nations whose words are not constructed from letters, but consist of particular and inseparable diagrams, *e. g.*, hieroglyphics of the ancient Egyptians and the word-writing of the east Asiatics (Chinese and Japanese), are evidently subject to different conditions. In this instance we must assume that only optic word images are stored up as memory pictures in the optic area, and, therefore, a lesion of the word idea, *a* + *b*, would not lead to the same disturbances of writing and reading as among Europeans, since in writing, the optic word images, avoiding the points *a* and *b*, are probably directly associated with the word idea. A similar condition occurs among peoples who make use of an alphabet with separate symbols for the numbers, *i. e.*, reading and writing of the latter may be intact in central aphasias, in which writing and reading (lesion at *a* + *b*) is severely disturbed. (See p. 1119.) The theory that the numeric symbols do not have the same position as the other characters, in that they are directly associated with the numeric concepts and avoid the points *a* and *b*, best explains this.

It follows that a language constructed from word symbols is much less complete than one founded upon an alphabet, since the acquisition and use of the former are a severe tax on the memory. It is not difficult to foresee how much greater would be the number of those who would forget the characters soon after learning them, or to whom the art of reading and writing would remain quite foreign, if we possessed a symbol language; this was surely the condition until lately among the east Asiatic peoples. The difficulties of symbol writing are somewhat analogous to the clumsy and comparatively useless method of printing by woodcuts before the invention of individual type. One may say that, in regard to science at least, the progress of nations is associated with letter language, just as the introduction of separate type rendered possible the advent of the renaissance, and in particular the progress of science. In spite of their centuries of civilization, the east Asiatic nations until recently have been absolutely dependent on Europe as the source of their scientific knowledge; a fact that is surely due to want of a letter language (a strong movement for its introduction is now under way in Japan); for it has robbed them for centuries of the most convenient and democratic means of acquiring and propagating scientific knowledge.

After what has been said, it is plain that written speech (including both the reading and writing of words) will always be affected if the word concept (*a* and *b*) be injured in any way, that is, if the lesion be situated at *a*, at *b*, or between *a* and *b*. This applies, on the one hand, just as much to reading aloud as to the comprehension of written speech; and, on the other hand, just as much to spontaneous writing as to writing from dictation. An interference in mechanical copying, however, in which one letter is pictured after the other, always depends upon a lesion in the territory of the writing arc (*ma/b*). Mechanical copying is something quite apart from the speech function. Like drawing, it is a sort of mechanical skill which depends upon the association of optic memory pictures and apperception, on the one hand, and upon the coördinated innervation of the hand muscles on the other. It is worthy of note that, because a lesion between *a* and *b* destroys the word concept, it makes writing quite impossible, or occasions a very marked defect in it, but never leads to paragraphia. The latter is analogous to paraphasia, and produces only a confusion of words in writing. Paragraphia occurs only in transcentral sensory aphasia (see below, 3), and according to the law that the complicated functions suffer the most, it may be very marked in cases in which paraphasia is insignificant.

The effects of the different kinds of aphasias on written speech (see p. 1105) are as follows[1]:

1. *Central* (*Cortical*) *Sensory Aphasia.*—Lost: voluntary writing to dictation, comprehension of writing, reading aloud. Retained: mechanical copying.

2. *Subcentral* (*Subcortical*) *Sensory Aphasia* (Pure Word-deafness of Lichtheim.)—Written speech is quite unaffected. This is very rare and may be confused with a high-grade diminution of hearing, especially as a certain diminution of the acuity of hearing may be associated with it. (See p. 1111.)

3. *Transcentral* (*Transcortical*) *Sensory Aphasia.*—Lost: comprehension of writing. Retained: reading aloud without comprehension, and writing in all its forms. Paragraphia (written paraphasia, see p. 1105, 3) is, however, present in spontaneous writing, *i. e.*, the words are confused, just as in speaking.

4. *Central* (*Cortical*) *Motor Aphasia.*—Lost: all forms of writing and reading, with the single exception of mechanical copying. See p. 1118, in regard to the persistence of apparently isolated agraphia in recovering cases. Von Monakow observed the capacity for writing preserved in a case in which a circumscribed lesion was found in Broca's center.

5. *Subcentral* (*Subcortical*) *Motor Aphasia* (Pure Word Dumbness).—Lost: reading aloud. Retained: writing in all its forms, and the comprehension of writing.

6. *Transcentral* (*Transcortical*) *Motor Aphasia.*—Lost: spontaneous writing. Retained: writing to dictation, copying, reading aloud, and the comprehension of writing.

7. *Conduction or Association Aphasia.*—Lost: all kinds of reading and of writing, with the exception of mechanical copying. Definite clinical cases of this sort are unknown. (See p. 1111.)

In these disturbances dependent upon aphasias, the writing and reading of individual letters are generally quite the same as the writing and reading of entire words.

[1] The numbers correspond to those in Fig. 438. (See p. 1108.)

The occurrence of mirror-writing in aphasia requires some mention in this connection. If a patient suffering from aphasia with paralysis of the right hand can write at all, *i. e.*, in subcortical motor, subcortical sensory, or transcortical motor aphasia (retention of word concepts), he will frequently write *en miroir*, instead of the usual script, when requested to write with the left hand. The phenomenon has been attributed to the aphasia, but, as normal individuals also possess a similar tendency to execute mirror-writing whenever they attempt to write with the left hand, such an explanation is manifestly incorrect. This tendency may only be overcome by a distinct effort of the will, and it is due to the fact that, in the use of the right hand, the left, through the associated acting of symmetric muscles, is unconsciously exercised in mirror fashion. Hence it is obvious that for hemiplegics, in whom the left hemisphere has been excluded by the paralysis of the right hand, it would become more difficult to master the inclination to mirror-writing.

The Real Anatomic Nature and Position of the Points and Lines of the Speech Diagrams, and the Anatomic Localization of the Individual Forms of Aphasia

Wernicke and Lichtheim have shown that an aphasic lesion, which has been localized theoretically in the psychophysic diagram (Fig. 438, p. 1108), may also be localized anatomically if we are familiar with the positions of the tracts and centers of the speech area.

In the first place, it is necessary to refer to the fact, demonstrated on p. 1101, Fig. 432, in the discussion of the relationship of Broca's, or the motor speech center

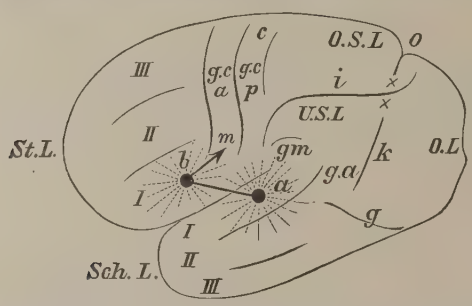


Fig. 439.—*c*, Central sulcus; *o*, parieto-occipital sulcus; *i*, intraparietal sulcus; *k*, anterior occipital sulcus; *g*, inferior occipital sulcus; *St.L.*, frontal lobe with its three convolutions (*I*, *II*, *III*); *g.c.a.*, anterior central convolution; *g.c.p.*, posterior central convolution; *O.S.L*, superior parietal lobule; *U.S.L*, inferior parietal lobule; *O.L.*, occipital lobe; *gm.*, gyrus marginalis; *g.a.*, gyrus angularis; *x x*, connecting gyrus between parietal and occipital lobes; *a*, *b*, and *m*, correspond to the letters in diagram 438. The dotted lines radiating from the points *a* and *b* represent transcentral association of ideas (Fig. 434, p. 1103.)

to the motor speech pathway, and first established by Marc Dax, that central speech is located normally in the left hemisphere only. Left-handed persons constitute the chief exception to this rule, since it has been demonstrated by pathologic findings that their central speech is a function of the right hemisphere. Normal left-sided speech is associated with the normal activity of the left hemisphere and of the right hand, although the reason for the wide-spread preponderance of the latter is still unknown. It is quite evident, however, that the unilateral localization of the delicate motor functions of the hand, as well as the more complicated speech function, indicates an economy of power for the brain. Schreiber has reported rare cases (see p. 1120) of aphasia in right-handed individuals in whom the faculty of speech was located in the right hemisphere. In other exceptional cases, cited by Wernicke, the aphasia disappeared, although a complete destruction of the left zone of language was subsequently demonstrated. In these cases a vicarious exercise of the speech function on the part of the right hemisphere must be assumed. As a matter of fact, a complete recovery from motor aphasia occurs only in children capable of education, whereas in sensory aphasia, the deficiencies are frequently restored, as Wernicke has shown, through the acquisition of word-memory pictures by the right hemisphere. This must not be confused with the disappearance of aphasias which have been caused by pressure instead of destructive lesions.

In regard to the centers and tracts assumed in the theoretic diagram, and without heed to the question of localization of the speech function on the right or left side, we have seen that Broca's or the motor speech center (*Ca* in Fig. 438, p. 1108) is situated in the foot of the inferior (third, according to the usual terminology, but first developmentally) frontal convolution, *i. e.*, the part next the anterior central convolution. The sensory, or Wernicke's center of speech (*b*, Fig. 438), is located in the posterior part of the superior and a contiguous part of the middle temporal convolutions. The path *bn* (motor speech tract, Fig. 438) represents an association tract, which passes from Broca's area to the psychomotor center in the faciolingual area, and penetrates only slightly the subjacent white matter. The association path, connecting the motor and sensory speech centers (*ab*, Fig. 438), passes through the region of the insula. These relations are represented in the anatomic diagram first, and the designations correspond to those of Fig. 439. The association tracts, *Ca* and *Cb* of Fig. 438, *i. e.*, connections between concepts and motor and sensory centers, have been indicated, as far as possible, in the same diagram. Fig. 434, p. 1103, shows these paths more accurately in their anatomic relation than the purely theoretic diagram of p. 1108. There are very many paths between the speech centers and all parts of the brain, where ideas and memory pictures are deposited, and, as it would be impossible to indicate them as lines in the anatomic figure, they appear as radiations from the points *a* and *b*. We must conceive them as spreading out over the

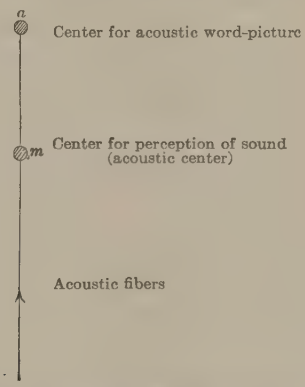


Fig. 440.—Probably an incorrect conception of the relations between the acoustic word-picture center and acoustic perception.

whole thinking part of the cortex, although, for the sake of simplicity, they are indicated for a short distance only beyond the points *a* and *b*.

This method of schematic representation shows that transcortical or transcentral tracts cannot be completely interrupted by an extensive lesion without implicating either of the corresponding centers, *a* and *b*. The insula and inferior temporal lobe also contain a large number of transcortical or transcentral tracts, which terminate in both motor and sensory speech centers, and a lesion of these causes the so-called unclassified aphasias.[1] Furthermore, as the path *ab* is not the only one passing through the insula, we have no reason to expect that a lesion of this structure could cause the purely theoretic and clinically uncertain picture of conduction aphasia.

The author believes that the acoustic tract (*ma*, Fig. 438) represents a group of fibers, a lesion of which causes the symptom-complex of subcentral sensory aphasia or pure word-deafness. Pure word-deafness is due to an interruption of the centripetal acoustic stimuli which arouse the acoustic word representation, and it consists in the loss of comprehension of spoken language, with integrity of the other speech functions and without pronounced deafness for other sounds. In the former editions of this work the author has assumed the tract *ma* to be a pathway connecting the center of the acoustic nerve with a special center for the acoustic word-memory images, as shown in Fig. 438.

[1] Naunyn, Cong. f. Med., 1887.

A division of the central organ of the acoustic nerve into a center for sound perception and a center for word-memory images is not in accord with the much simpler theory that ideas caused by association and perceptions resulting from sensory impressions, are localized at the same time in the cortex, and are differentiated by the kind of excitation only. The latter theory has never been disproved by pathologic study. The radiation of the acoustic fibers toward the cortex also renders such a division purely hypothetic and superfluous for the explanation of subcentral sensory aphasia. As a result of many studies, it may be regarded as settled that each acoustic nerve is connected with both hemispheres, thus following in its central course the type of bilateral innervation of most cranial nerves, and possessing a semidecussation like the optic, for example.

The optic tract terminates primarily in the pulvinar, the anterior corpus quadrigeminus, and external geniculate body; in a similar manner the acoustic fibers terminate primarily in the posterior corpus quadrigeminus and the internal geniculate body of the same side; the then impulses pass onward, through the brachium conjunctivum and stalk of the geniculate, to the first and second convolution of the temporal lobe. The central part of the acoustic fibers above the decussation thus contains fibers from both acoustic nerves, and we may complete the analogy to the optic tract, and call it the acoustic tract.

A unilateral lesion of the temporal lobe or of the fibers of the acoustic tract (lesion x and y, Fig. 441) does not cause unilateral deafness, as may be seen from the

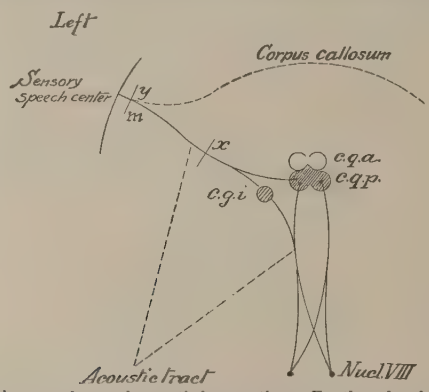


Fig. 441.—Diagram of central acoustic innervation. For the sake of clearness the right acoustic tract is represented only so far as the primary acoustic center. It must be imagined as terminating on the right side of the diagram in the cortex and communicating with the callosal fibers.

figure. At most, it can only cause a moderate diminution of hearing in both ears, hard to demonstrate, because both acoustic organs are still in communication with the hemisphere opposite the lesion. On the other hand, the symptom-complex of subcentral aphasia does not follow any arbitrary lesion of the left acoustic tract, *e. g.*, near the posterior corpus quadrigeminus, (x, Fig. 441), as clinical observations will show. The lesion must be located either in the cortex of the left temporal lobe (Veraguth's case) or in (lesion y, Fig. 441) its immediate vicinity (Liepmann's case). The theory which best explains this is that the sensory speech center receives acoustic stimuli circuitously from the right temporal lobe in addition to those passing along the left acoustic tract, and that these two sets of stimuli can be simultaneously interrupted only at a joint near the cortex of the left temporal lobe. The connection of the sensory speech center with the right temporal lobe occurs through the corpus callosum, and is indicated by the dotted arc in the accompanying figure. y represents the meeting point of the stimuli, coming from the right temporal lobe, with those of the left acoustic tract, and a lesion at this point only will cause subcentral word-deafness. There need be no more than a slight reduction of hearing in such a lesion, as the diagram will show, because each acoustic nerve is still in communication with the apperceptive center of the right side. The path *ma* (Fig. 438) represents anatomically the sum of the fibers of the left acoustic tract plus the callosal acoustic fibers. The point in the anatomic diagram (Fig. 441) where the fibers of the left acoustic tract and of the corpus callosum meet, a lesion of which (y) causes subcen-

tral aphasia, corresponds to the letter *m* of the theoretic diagram (Fig. 438), although the latter cannot be indicated in the surface view of the brain. With the exception of Liepmann's case, in which a subcortical lesion of the white matter seemed to be the anatomic cause of a pure word-deafness, the lesions have thus far been found either in both temporal lobes (Dejerine) or else in the cortex of the sensory speech center, and this agrees exactly with the author's conception. In Dejerine's case the lesion of the left side evidently destroyed the fibers of the acoustic tract, and that of the right destroyed the callosal connection between the two temporal lobes. The lesion in Veraguth's case, on the other hand, although cortical, was of such a nature that it did not totally obliterate the sensory speech center, but interrupted the conduction of impulses to it instead (just as at *y*, Fig. 439). There is a well-known analogous condition in motor aphasia, *i. e.*, when the symptom-complex of subcentral motor aphasia is due to a small circumscribed lesion of Broca's area. Here, again, the motor speech center is obviously not affected, but simply the association tract leading to the faciolingual area in the anterior central convolution (*bn*, Fig. 439, p. 1110). The author believes that observations of this sort warrant the substitution of the term subcentral for subcortical.

The isolated disturbances of written speech do not really belong to true aphasia, and the nature and position of the tracts *aa* and *ba* will be discussed in the following section.

The So-called Isolated Disturbances of Written Speech Independent of Aphasias (Isolated or Literal Alexias or Agraphias)[1]

Besides disturbances in writing and reading dependent upon aphasias, there may also occur disturbances of written speech which are independent of the aphasias. This will be the case when a lesion occurs in the lower part of the diagram (Fig. 438), *i. e.*, in the writing arc and in its connections with the central speech apparatus (in the radius of lesions, 8–14).

These disturbances, as contrasted with those depending upon aphasias, may be termed *isolated alexias* and *agraphias*. According to the diagram, seven such disturbances are theoretically possible, for which a similar terminology may be employed as for the aphasias (Fig. 438).[2]

8. *Subcentral Alexia* (Injury between μ and a; "Pure Literal Blindness").—Reading of letters and words impossible; writing of letters and words, with the exception of copying, possible.

9. *Subcentral Agraphia* (Injury between β and v).—Reading of letters and words retained, but words can neither be written nor copied. (See below for the significance of this form.)

10. *Central (Cortical) Alexia* (Injury at a).—Letters and words can neither be written nor read, and even copying is impossible.

11. *Central (Cortical) Agraphia* (Injury at β).—Letters and words can be read but not written nor copied (as in 9). (See below for the significance of this form.)

12. *Conduction or Association Agraphia* (Injury between a and β).—Letters and words can be read but not written nor copied (again as in 9 and 11). (See below.)

13. *Transcentral (Transcortical) Alexia* (Injury between a and a).—Reading of letters and words impossible. Writing of letters and words, including copying, possible.

14. *Transcentral (Transcortical) Agraphia* (Injury between b and a).—Reading of letters and words possible. Writing of letters and words, except mechanical copying, impossible.

In the narrow sense of the word, lesions 9 and 11 do not actually come under the head of the agraphias, because the agraphias here depend only upon a paralysis of the arm.

Therefore, only lesions 12 and 14 are to be considered as isolated, pure agraphias, and they can be distinguished one from the other by the retention of the power of copying in 14, and its loss in 12.

[1] It is better to limit the terms alexia and agraphia to the disturbance of written speech, which, in the usual acceptation of its term, are independent of aphasia. As literal disturbances of written speech they may be contrasted with verbal disturbances due to aphasia, since Wernicke (Das aphasische Symptomcomplex, Deut. Klinik, 1906) has shown that just as reading and writing among European folk occur by spelling, so disturbances of reading and writing affect not merely words, but also letters.

[2] The numbers correspond to those in Fig. 438.

The three alexias, 8, 10, and 13, can be differentiated one from the other by the fact that in 13, as opposed to 8 and 10, copying is retained, and that in 8, as opposed to 10, spontaneous writing is retained.

The forms of isolated alexias and agraphias, considered here theoretically, have thus far rarely been observed as pure cases, but much more frequently there occur *mixed forms* arising from diffuse injuries to the cortical mechanism of speech writing or from the combined injury of two or even more of the opposite convergent tracts in the neighborhood of the decussation angle. For this reason, and on account of incomplete interruptions of conduction, a local diagnosis of alexia and agraphia disturbances often becomes very difficult or even impossible.

Only two of the isolated alexias and agraphias have attained a sure place in clinical medicine, namely, the form of pure alexia referred to at 13, Fig. 438, p. 1108, and the combination of alexia with agraphia according to disturbances 13 and 14 of the text. If we start from the optic writing center a, they should be termed transcentral, but if, as Wernicke prefers, we start from the center of tone speech, they should be called subcortical or subcentral. These two types have been so carefully studied, both anatomically and clinically, that we are able to evolve the anatomic nature of the mechanism of writing and reading.

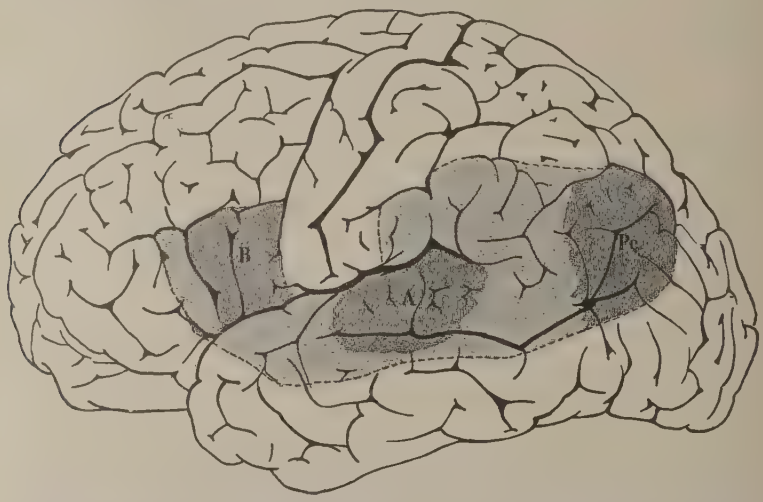


Fig. 442.—Lateral view of the left cerebral hemisphere according to Dejerine. The zone of language is shaded: *B*, Broca's convolution, seat of motor word-image; *A*, Wernicke's convolution, seat of acoustic word-image; *Pc*, pli courbe, gyrus angularis, Dejerine's seat of optic word-images (see text).

Whatever has been said concerning the mechanism of writing, in the region below the line *ab* of Fig. 438, p. 1108, and the isolated literal alexias or agraphias, *i. e.*, those independent of aphasia, has only a theoretic value, because the author's diagram of the central mechanism of writing is purely theoretic. But, just as in the explanation of true aphasia, it now becomes necessary to ascertain the anatomic meaning of the centers $a\beta$ and the association tracts, $a\alpha$, $b\alpha$, and $a\beta$ of Fig. 438. According to Fig. 437, p. 1107, we may assume that the point β in the anterior central convolution is the motor center for the usual manner of writing with the right hand, and that it can be replaced by any other motor center if other parts of the body be used for writing. As we have already (p. 1107) dispensed with an actual center for writing, it is evident that the path, βv, is simply the corresponding motor pathway, *i. e.*, the pyramidal fibers belonging to the right arm. Moreover, the whole question hinges on the conception of the center a. The typical symptom-complex of isolated or literal alexia or a combination of literal alexia with agraphia, without essential disturbances of speech, is regularly associated with lesion of the left temporal lobule, especially the gyrus angularis. It was, therefore, most convenient to assume, with Dejerine, that an isolated optic word center existed in the left gyrus angularis, a

lesion of which, or its dissociation from the other speech apparatus, would cause this symptom complex. Fig. 442 shows this localization according to Dejerine's conception.

This conception is altogether untenable, since, as we have seen on p. 1108, written speech is represented in the cortex, not as entire optic word-memory pictures, but rather as letter images. In reading, the function of the organs of internal speech is to construct these letter images as (acoustic) word concepts. In writing, a series of optic letter concepts is reproduced through the disintegration of the word conceptions. If, therefore, an optic center in the left hemisphere must be assumed, it can only be a center for optic letter images. But we must follow Wernicke further in the criticism of this view, and deny the existence of a left-sided optic speech center altogether, even though it be for letters only. We have sure proof, from observations on right-sided hemiopia, that optic letter memory pictures are deposited in both hemispheres, and that they behave just as other memory images do. If optic letter memory pictures were deposited in the left hemisphere only, as one was inclined to deduce from cases of isolation alexia and agraphia, alexia must necessarily appear in right hemiopia caused by interruption of the left optic tract, the left hemisphere obviously being blind. We know, however, that this is not the case, not even temporarily. Hence the excitation from the right hemisphere must be sufficient to arouse optic letter images in reading, and to associate them with the organs of central speech. This obviously depends on the fact that the fixation-point is represented in both hemispheres, and that central vision hardly suffers at all in hemiopia. The assumption of a peculiar and individual optic speech center, in the sense of an optic letter center a in the left hemisphere, Fig. 438, is purely fictitious for the sake of easy comprehension, and Dejerine is not warranted in according it an anatomic position. As a matter of fact, to explain isolated alexias and agraphias, we must consider a as two centers, placed symmetrically on either side of the middle line, in the optic region, *i. e.*, occipital lobes of the left and right hemispheres.

But how do the anatomic findings mentioned above, *i. e.*, lesion of the left angular gyrus, which produces isolated alexia, create the impression of a left-sided optic speech or letter center? Obviously, because the letter memory pictures,[1] have of themselves no meaning, and acquire importance only through association with the acoustic letter or sound concept, *i. e.*, the acoustic speech center, which is localized exclusively in the left side. We, therefore, conclude that the occurrence of alexia in lesions of the left gyrus angularis is in no way due to the fact that the ideas of letters are disturbed (this is impossible, because, as we have seen, the optic letter memory pictures are stored in both hemispheres), but is due to an interruption of the association of these optic letter memory pictures with the acoustic speech center of the left side. The anatomic conditions of the white matter of the gyrus angularis are such that a lesion may have this effect, as Fig. 443, p. 1116, will show. According to the figure, the white matter of the temporosphenoidal lobe, including the gyrus angularis, contains three principal fasciculi, namely, the fasciculus longitudinalis inferioris, which connects the cortex of the temporosphenoidal lobe or the acoustic word center, with visual center of the occipital lobe; the callosal fibers, which connect the acoustic word centers of the left side with the right temporal and the right occipital lobes; and the optic radiations, passing from the posterior border of the internal capsule to the visual center of the occipital lobe on the same side.

According to von Monakow's and Wernicke's investigations, these fasciculi appear in close contact at the point (lesion y, Fig. 443) where pure alexia is usually localized. A lesion at this point, therefore, interrupts, first of all, the left optic radiations, and by isolating the left hemisphere, *i. e.*, the left depot for letter memory pictures, from the external world causes the right temporal hemiopia that has so far always been associated with alexia. Consequently, in attempting to read, this source of apperceptions becomes closed. Normally, however, there remain the stimuli from the right occipital lobe, which reach the acoustic word center by means of the optic acoustic callosal commissural fibers. (See Fig. 443.) The lesion y interrupts this pathway also, and the acoustic word center is thus closed to every sort of optic stimulus. As a result, we have alexia. The lesion y corresponds in its

[1] It would be really better to speak of optic oculomotor letter memory images, because the essential characteristic of optic letters is the representation of the linear direction taken by the letters. As the cortical area of the opticus stands in close interrelation with the motor centers of the ocular muscles, this feature must depend on the association of the image with the representation of ocular movements belonging to it.

effect to lesion 13 of Fig. 438, p. 1108, and it is designed to show, unnecessarily perhaps, that, in addition to the left optic radiation, there is interruption of the association between optic and acoustic centers of the left side (fasciculus longitudinalis inferioris) as well as the connection between right and left auditory centers (bitemporal callosal commissure). Although this adds nothing to the clinical picture, it is conceivable that in rare instances the symptom-complex of alexia may occur without destruction of the optic radiations, *i. e.*, without hemiopia. Thus it might happen that merely the connection between the left temporal lobe and both occipital lobes (fasciculus longitudinalis inferioris of the left side and the optic acoustic callosal fibers coming from the right side) was destroyed. In this instance, the acoustic word center would still be closed to all optic stimuli. It should be mentioned that lesions of the left gyrus angularis causing pure alexia occur, as a rule, through embolus of the posterior twig of the third branch of the Sylvian artery.[1]

Blindness for musical notes has also been observed as another detail of the clinical picture of pure or literal alexia. (See p. 1123.) By this is meant the addi-

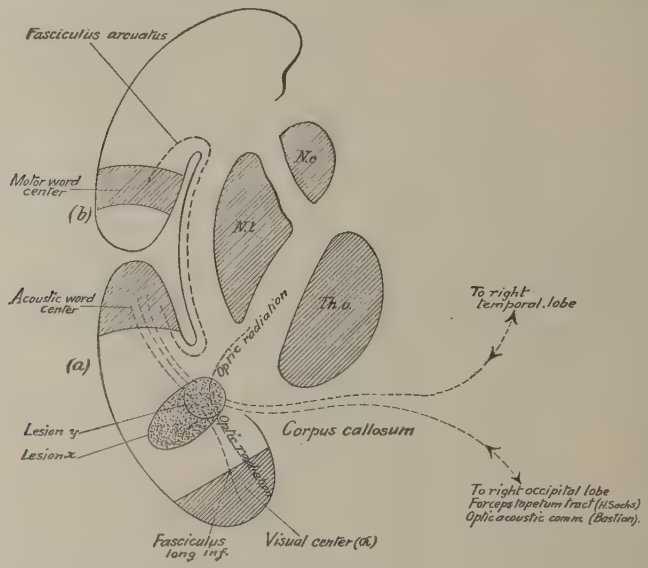


Fig. 443.—Diagrammatic representation of literal alexia and agraphia. Lesion *y* causes pure alexia; lesion *x*, alexia with agraphia; *NC*, nucleus caudatus; *Nl*, nucleus lenticularis; *Th o*, optic thalamus. The structures concerned in literal alexia are represented diagrammatically by a horizontal section through the superior end of the fissure of Sylvius.

tional loss of the comprehension of musical notation and the ability to sing by note; it is really alexia for musical notation.

The cases of alexia which we have thus far discussed have not been associated with agraphia, because the communication between the motor speech center, the depots for optic letter memory pictures (of both hemispheres), and with the motor center of the right hand, has been preserved. It has been occasionally observed that patients are able to overcome or avoid alexia by carefully tracing the letters with the finger. This enables them to read aloud with comprehension. In this instance the mechanical act of copying reverses the process of voluntary writing, and thus awakens the idea of the word (from *a* to *b*, Fig. 438, p. 1108). Magnan has described a case of isolated alexia which had the remarkable peculiarity that the patient was unable to read, either by sense of touch or by the optic tract, although raised letters were employed, on account of lack of practice with letters used by the blind. It is explained by an interrupted communication between the tactile

[1] See von Monakow, Gehirn-Pathologie, Nothnagel's Sammelwerke, 1897, p. 673.

representations (most probably located in the central convolutions and the parietal lobe) and the acoustic speech center. The ability to find the right word is commonly involved in isolated alexia, to such an extent that it resembles aphasic disturbances and may lead to a false conception of the case. In the latter instance this depends on the fact that there is not only a disturbance of the association of the letter image with the acoustic word image, but also the association of other (objective) optic impressions with the entire acoustic speech center. (Relation of Alexia to Optic Aphasia, see p. 1119.) As we take the ground that the optic letter memory images are in no way different from the other optic memory pictures, this is perfectly clear. For the same reasons, it is quite evident that so-called pure alexia may be associated occasionally with a certain degree of psychic blindness, because the left hemisphere has already been deprived of the impressions (through the hemiopia), whereas the right hemisphere has lost although not completely, the most important association paths for the recognition of objects, *i. e.*, for word conceptions. From this detailed description of the symptom-complex it is evident that its designation as pure alexia is to be taken *cum grano salis*, and only signifies that it is an alexia not dependent on a primary disturbance of acoustic speech. When the disturbance at the point y (Fig. 443) is incomplete, or when there is only a functional disturbance due to the remote effect of a lesion in the vicinity, instead of alexia, we observe the clinical picture of dyslexia, *i. e.*, difficulty in reading with rapidly appearing fatigue, which often leads to complete inability to read and a consequent disinclination to read on the part of the patient.

In addition to the so-called isolated alexias, the combination of alexia with agraphia is practically the only disturbance of written speech among the theoretic possibilities considered (p. 1113), due to a lesion of the arc of writing (Fig. 443), rather than to a disorder of spoken language. A glance through the literature will show that in these cases also lesions in the gyrus angularis are found. According to Wernicke, however, they differ in that the lesion is more extensive than in the former, and approaches the cortex more closely, as lesion x (Fig. 443) will show. The appearance of agraphia in these cases is to be explained by the theory that, in consequence of the greater extent and less circumscribed position of the lesion, either the pathway which connects Broca's center with the optic center (Fig. 438, p. 1108), or else the tract between the optic center and the motor center for the right hand ($\alpha\beta$, Fig. 438) must be destroyed. In the second case, the patient could still write with the left hand, whereas in the first the ability to write would be lost for all parts of the body.

We know very little as yet concerning the anatomic character and position of the tracts assumed to be involved when agraphia appears, and the author has purposely refrained from indicating them theoretically in Fig. 443. The disturbances of writing and reading in this combination differ from the disturbances of written speech, which accompany true aphasias, in that verbal disturbances, *i. e.*, writing and reading of words, are not more predominant than the literal disturbance, *i. e.*, writing and reading of letters. Thus, for example, letters cannot be copied mechanically, as they are not recognized, and cannot be transposed from one style to the other. But if we except mechanical copying even the true aphasic, under certain conditions, *i. e.*, severe verbal disturbances of writing and reading, cannot always do this.

By means of these clinical pictures we can understand the anatomic nature of the diagram of writing ($\alpha\nu\alpha\mu\beta\nu$, Fig. 438), but the position of the tract $\alpha\beta$ is still an open question. A lesion of this tract (lesion 12 in Fig. 438) should cause isolated agraphia. But since, as far as the author knows, such a case without alexia and without aphasia does not exist, no definite assertion may be made concerning its position. Von Monakow considers it probable that the fasciculus longitudinalis superioris of the cortex contains the association fibers between the optic centers for letters and the motor region, although this is purely hypothetic. That isolated agraphia has never been observed is probably due to the fact that the tract $\alpha\beta$ is placed bilaterally, corresponding to the bilateral deposition of letter images, and hence a unilateral lesion cannot disturb this function. This leaves quite out of consideration the fact that each optic center is not merely associated with both hands, but with multiple motor tracts, as we can write with every part of the body (Fig. 437, p. 1107).

Wolff has described a curious form of combined alexia and agraphia without aphasia in which there was a double cortical blindness. The patient could neither write nor read, since both of the optic zones were destroyed, the first because of blindness, the second because the letter concepts and all their associations were disturbed.

Although reference has been made in the preceding paragraph to the absence of

agraphia without alexia, cases *resembling* pure agraphia are really not so uncommon. A careful history, however, will very soon show that they are really the vestiges of a receding aphasia. In fact, an isolated residual disturbance of writing is not at all uncommon during recovery from a central motor aphasia (Broca's), at the time when the speech faculty is either completely or almost completely restored (in these cases we are probably dealing with remote effects without actual destruction of the centers, or with the assumption of function by the right hemisphere seen only in children). The reason for this lies in the fact that the motor speech center has recovered the easier function of speech, whereas the more difficult act of writing (more difficult because the impulses must pass over a greater number of neurons) is still defective. Without proper histories, these cases may very easily give the impression of independent agraphia; but it is just in these cases of mild functional disturbance, rather than complete destruction of Broca's center, that the verbal, and not the literal, character of the agraphia is demonstrated by examination. For such apparent isolated agraphia, the author would suggest the name aphasic residual agraphia.

The Mixed and Unclassified Forms of Aphasia; Functional, Amnesic Aphasia.—The Real Nature of Transcortical Aphasia.—It should also be noted that the diagnosis of individual cases is often made very difficult in aphasias by the occurrence of such mixed forms from lesions of the converging tracts, as well as by the occurrence of incomplete lesions of individual tracts and centers and of diffuse lesions. Hence every case of aphasia cannot be tabulated under one or the other of the above types; at all events, not without much difficulty.

There is still another reason why, practically, aphasias are often more difficult to explain than one would judge from our simple diagram. For in addition to the above-described type, where the disturbances depend upon injuries to tracts and destruction of centers, there is still another group of aphasias in which the difficulty is merely functional in nature and the tracts and centers in question are not actually destroyed or even injured. Such aphasias depend upon a very difficult or an imperfect innervation of the center and tracts upon the part of the patient. From the nature of the trouble, the clinical picture not only varies so conspicuously as to make a local diagnosis difficult, but also presents many other peculiarities. Under this head come the aphasias which are attributed to a disturbance of the memory, as the following case of Grashey will illustrate. This patient could give the name to an object held in front of him only so long as he was looking at it, and even then only while he was writing down its name and thus aiding his memory. These aphasias from disturbances of memory have been considered fundamentally different from the other aphasias, but the author cannot agree with this view. For what do we actually understand by a disturbance of memory? Apparently, on the one hand, only a difficulty in voluntarily recalling certain latent memory pictures, *i. e.*, a difficulty in associations, and, on the other hand, an abnormally rapid fading of concept soon after their origin. Between these conditions and a complete destruction of the association fibers or of the concept centers there is only a difference in degree. Such destructions depend upon appreciable anatomic lesions, while disturbances in memory are to be attributed only to slight functional damage to the same centers and tracts.

By adhering to this definition of disturbances of memory, we can term these functional aphasias *memory aphasias* (in Grashey's sense), in contrast to aphasias from destructive lesions.[1] The former, however, include not only Grashey's and similar cases, but, as will be easily understood, most of the transcentral and especially the complete transcentral aphasias. In a complete transcentral motor aphasia, which is the direct consequence of a gross anatomic lesion, all tracts which lead from *a* and *b* in Fig. 434 to the partial representations of the idea must be interrupted. But since these partial representations of the idea are spread out in the entire cortex, we must assume that the fibers *bc*, *bc″*, *bc⁗*, etc., in reality extend in all directions from the speech centers (Fig. 439). A complete interruption of conduction of these collected tracts could then be imagined only if the centers, *a* and *b*, were to a certain extent isolated, as by a ring-shaped lesion. However, in assuming a gross anatomic lesion, it is quite impossible that the centers *a* and *b* could remain intact, so that symptoms of a central instead of a transcentral aphasia must result. It is, therefore, evident that complete transcentral motor aphasia and, for similar reasons, even a

[1] Central and transcentral aphasias, dependent on anatomic lesions, in which difficulty of finding words simulates memory weakness, should not be confused with amnesic aphasias due to disturbances of memory or function. The cause of this phenomenon is different and depends on the fact that the word cannot be found or spoken, because the impulses travel only the path *Cb* and not *Cab* at the same time.

transcentral sensory aphasia, cannot arise from direct gross anatomic destruction of all the transcentral tracts. A complete anatomic destruction of the latter is absolutely impossible without a lesion of the center *b* or of the center *a*.[1] But from what has been said, it is easy to understand that these transcentral disturbances may result from those functional lesions defined above as disturbances of memory.

Such a functional disturbance may, of course, be diffused not only to the tracts of the speech mechanism, but also over the entire brain. In the former case merely a memory disturbance of speech will result; in the latter, a general weakness of memory and intelligence, of which the aphasia is only a part.

Most of the disturbances of speech called *indefinite* or *diffuse aphasias*, as contrasted with the definite accompanying functional lesions. They include aphasias which can be explained, not by a lesion at definite places in the scheme, but only by the assumption of a disturbance diffused over the territory of the speech apparatus. Such aphasias usually present an exceptionally variable character, and so cannot be attributed to the direct action of gross anatomic disturbances, although anatomic mixed aphasias may have the character of a diffuse aphasia. (See p. 1118.)

It should, however, be noted that in designating certain aphasic disturbances as *functional*, we do not mean that they cannot occur from the remote action of gross anatomic lesions. On the contrary, indefinite and transcentral aphasias, which, according to the above definition, must be considered as functional, generally exhibit lesions in the neighborhood of the speech centers. There is no actual destruction of brain substance in a gross mechanical sense, but the lesion indirectly causes a functional disturbance of the speech apparatus from *remote action*. This remote action, playing so important a part in other parts of the cerebral pathology, is, as is well known, to be attributed partly to the results of circulatory disturbances, partly to inhibition.

Although most transcentral aphasias can thus be considered as functional, or, in the sense above, as of an amnesic nature (arising from weakness of memory or of association), such a grouping does not necessarily include those transcentral aphasias in which not all the transcentral tracts uniting the conceptual part of the brain with the speech center, but merely a certain number of transcentral tracts of separate function, are affected. To this class belongs Freund's so-called optic aphasia, in which the patient cannot name objects after he has received their optical impression. Here we must assume an isolated lesion of the fibers running from the visual center to the motor speech center. Such a lesion may be anatomic as well as functional. In the cases described up to the present, however, a coincident hemiopia, has always been found, and sometimes even word-deafness. In the examination of optic aphasia, psychic blindness should always be looked for at the same time, because optic aphasia may be merely an associated symptom of general psychic blindness (p. 1123). One must also determine whether or not the patient recognizes objects by sight. Up to the present time the anatomic findings in optic aphasia have regularly revealed lesions in the white matter of the left occipital lobe. This is easily understood, since an interruption between the motor speech center and the optic partial concepts must be the cause of the symptom-complex. Concerning the relations between optic aphasia, alexia, and psychic blindness, see p. 1123. The terms *acoustic* and *tactile* aphasia have meanings analogous to that of the expression *optic aphasia*.

Finally, it may be mentioned that in aphasia, numbers are effected like other words only when they are spoken, not written. Numbers expressed in figures occupy a peculiar place in written speech, because no real word concept of them occurs either in writing or reading. The figure is a direct symbol of the notion of counting; to a certain extent, a hieroglyphic. Its optical representation probably may be considered as directly associated with the conception (Fig. 438). Hence, even when the word concept in aphasia is destroyed, the patient can write figures quite well and can understand written figures.

For the explanation of *anarthria* as a result of incomplete aphasia, *i. e.*, of incomplete lesions of the central speech apparatus and of receding aphasias (central anarthria), p. 1101 et seq. may be consulted. In another type of incomplete aphasia the difficulty is limited to certain definite words. These are forms in which ordinarily no definite location in the speech mechanism is possible, and which usually come under the head of the functional or diffuse disturbances (p. 1118).

Criticism of P. Marie's Conception of Aphasia and the Disturbances of the Intelligence in Aphasia. The Author's So-called Logasthenia (Mihi).—P. Marie,[2] through ob-

[1] As we shall see below, it must be acknowledged that transcentral aphasias may arise directly from gross anatomic lesions by so-called remote action.

[2] Sem. méd., 1906, No. 21.

jections that are neither new nor, in the author's opinion, valid, has recently sought to overthrow the doctrine of aphasia given in this book, and the one generally accepted in Germany. This work is based on the well-known fact that, in a few isolated cases of central or cortical aphasia, no lesion of Broca's center has been found, and that, conversely, no aphasia followed a lesion of this area. This leads him to contest the localization of the motor center of speech in Broca's area. A refutation of Marie's arguments will be found in Naunyn's exposition of aphasia at the Medical Congress for Internal Medicine, 1889. He has shown that the greater part of these cases were not examined carefully enough, and that certain of them, showing Broca's area to be intact, were either not cases of this form of aphasia, or else were to be explained by a functional disturbance of the right hemisphere. Schreiber has shown that not merely left- but right-handed individuals as well, may have the aphasic lesion in the right hemisphere. Naunyn also points out that absence of aphasia following a lesion of Broca's area might be due to the fact that the speech center was situated in the right hemisphere. Certain it is that such apparently exceptional cases should be examined microscopically before they are accepted, since it is well known that decided hemiplegias occasionally show no macroscopic lesion in the brain. Furthermore, Naunyn's graphic record of the great number of cases in which the preponderance of probability places the location of the motor speech center in Broca's area, and that of sensory speech in Wernicke's area, furnish important evidence against Marie. The latter, relying on the exceptional cases which do not overthrow the rule by any means, removes with the stroke of a pen Broca's center, one of the landmarks of medicine that we have hitherto regarded as one of the greatest achievements of science. Marie reaches the following remarkable conclusion: that there is merely one kind of aphasia, although it is capable of great quantitative variations. It is localized in Wernicke's area and its distant and immediate vicinity, and consists essentially in a diminution of the intelligence necessary to speech. In the severest cases, this disturbance is so great that there results a complete lack of comprehension of spoken words, *i. e.*, the picture of Wernicke's sensory aphasia. In milder cases the defective intelligence is revealed only in a difficulty of comprehension, so that the patient can understand and execute simple uncomplicated commissions alone. He attempts at great length to prove that these disturbances of the comprehension of speech are really due to defective intelligence, by arguments based on the well-known fact that aphasics always exhibit some defective intelligence. The various forms of aphasia, to the establishment of which we owe so much to Lichtheim, Marie considers as merely higher or lower grades of this defect of intelligence, and maintains that their variations cannot be more closely analyzed. This is a statement which may be absolutely refuted by the fact that a great number of these cases can be sharply differentiated. Marie designates severe disturbances or loss of motor speech (motor aphasia) as anarthria; but if, in addition to this, there are sensory manifestations, *i. e.*, "defective intelligence" he calls the condition aphasia complicated by anarthria, and refers it to a lesion of the lenticular region [zone lenticulaire. —Ed.] This jumbling of motor aphasia and anarthria appears absolutely unjustifiable to the author; especially the localization of anarthria in the lenticular region. The author believes that Marie's doctrine indicates a decided step backward, and that it should not be accepted rashly; furthermore, that we are not justified in drawing the far-reaching conclusions from the exceptions to Broca's localization in central aphasia that Marie does, since these exceptions may be explained differently. The disturbances of intelligence, so constant in aphasia (even of the motor type), were recognized long ago and cannot be denied. But it does not necessitate the conclusion that it is the cause of the aphasia, and that the latter is merely a result of a peculiar form of defective intelligence, for it is perfectly obvious that the latter may result from the aphasia. All our higher processes of thinking take place in the form of interior language, as every one may demonstrate on himself, and it is very probable that they suffer considerably from the speech defect. To the author, it seems likely that the patients in whom these peculiar psychic defects arise, as a result of the speech disturbance rather than the cause of the same, appear not exactly idiotic or stupid, but in the condition of highly intelligent animals, capable of emotions of a finer type, even of reasoning power, in spite of the lack of speech, but who, on account of the lack of internal language, are without certain higher psychic functions. The author suggests that, since this higher faculty of thinking, which is associated with interior language, is peculiar to man, and is the chief point of differentiation between the animal and human mind, it should be called *logos*, and a disturbance of it, *logasthenia*. In the author's opinion, it is a result and not the cause of aphasia. This is supported by the fact that, as the interior language is undisturbed in subcentral or subcortical forms of aphasia, there is

no logasthenia. The greater relative frequency of the so-called unclassified aphasias —*i. e.*, those that cannot be sharply localized according to the Wernicke-Lichtheim scheme—is no argument against the correctness of the author's psychophysical and psychopathologic plan; on the contrary, if we consider the ultimate physiologic connection of all the widely separated parts of speech mechanism, it is not difficult to understand.

For further details, the discussion on Marie's conception of aphasia in the Société de Neurologie de Paris (Revue Neurologique, 1908) should be consulted.

(*c*) Other Speech Disturbances from Paralytic Phenomena

Anarthria and aphasia are the best known and the best studied of the disturbances of speech resulting from paralytic phenomena. There are, however, a number of other speech disturbances to be regarded as paralytic phenomena which are not yet exactly explained and, in fact, cannot be definitely localized.

The disturbance of speech in *progressive paralysis*, which is characterized by syllable stuttering, belongs to this class. From its peculiarities it belongs rather to the anarthrias than to the aphasias, and is ordinarily so classed; but it is questionable whether such a classification is correct. The well-known anatomic localization of progressive paralysis in the cerebral cortex makes it most probable that the speech disturbance is also cortical. Such a conception of its origin would suggest a closer relation to the aphasias, despite the external difference, and, according to the classification on p. 1101, it must be called central anarthria. As a matter of fact, such a disturbance of speech may perfectly well be conceived to arise from minute lesions in the area of the speech center, by which speech coördination is destroyed, although a complete paralysis of the center does not result. Perhaps the disturbances of speech in intoxicated persons may be similarly explained. Without doubt the *hysteric speech disturbances*—hysteric aphonia (improperly called hysteric vocal-cord paralysis) and hysteric mutism, should be localized in the cortex, and, therefore, despite clinical differences, are closely related to aphasia. *Congenital dumbness* is nothing more than motor aphasia, and deaf-mutism is sensory aphasia plus motor aphasia plus deafness. The imperfect monotone speech which deaf-mutes can be taught may be considered as a form of speech arising, with sensory aphasia, by arduous and unusual paths, in which, instead of the entire word concept $a + b$, there is only available a motor word representation. The different disturbances of speech of those who are seriously ill (the vibrating, tremulous, slowed, and abnormally faint speech) have not as yet been definitely localized. They may be central as well as peripheral. The characteristic scanning speech of *multiple sclerosis* and the speech defect of *Friedreich's ataxia* do not yet possess a definite significance. The former, perhaps, may be regarded as a sort of spastic gait of the speech. As a result of the increased muscle and tendon reflexes, which may frequently be demonstrated in the muscles of speech in this disease (jaw-clonus, etc.), the speech movements are mechanically hindered by the occurrence of spasms of the muscles, which the patient instinctively tries to overcome by slowing his speech and accentuating its movements. The monotone and the lack of the ability to modulate the voice may also be explained by such spastic phenomena. Ordinarily, the speech does not become tremulous, as do the other spastic movements, although a tremor may sometimes be observed as a result of quivering contractions of the vocal cords. This is probably due to the fact that the muscles of speech run in all the directions of space, and that tremors can be produced only by the alternate activity of antagonistic muscles, the lines of whose action are situated in the same plane.

3. AFFECTIONS OF SPEECH FROM IRRITATION PHENOMENA

These irritation or spasmodic phenomena in the territory of the speech apparatus have been much less studied than the speech disturbances thus far described, and which we have considered paralytic.

They include the commonest varieties of stuttering (labiochorea and guttural tetanic stuttering), both of which are sufficiently defined by their names. They also include the affections of speech in chorea. It is not yet clear how these disturbances arise, nor is it known from what point the impulses spring, although they probably have a cortical localization. It is not necessary to assume that they come from the speech center. This would be at variance with the conception of chorea on p. 959. For, as the speech muscles are not utilized exclusively for speech and are not innervated exclusively by the speech center, it is easy to understand that choreic movements of the speech muscles might arise from other parts of the cortex and still affect the speech. The tracts concerned in this are mentioned on p. 959.

4. PLAN FOR TESTING THE FUNCTIONS OF SPEECH

The following plan for examining patients with speech disturbances has been devised from what has been said above:

1. Disturbances of pronunciation of letters and then of simpler and more complicated words. Anarthritic disturbances of bulbar paralysis; speech disturbances of progressive paralysis; of multiple sclerosis; stuttering, etc. For the differential diagnosis between pure anarthria and what is called on p. 1102 "central anarthria," it must be noticed whether disturbances other than those of speech (swallowing, masticating) occur in the region of the speech muscles.

2. In the actual aphasic disturbances the following functions should always be examined:

(*a*) Test for Words

1. Voluntary speech. Examination for naming and paraphasia (word confusion).
2. Repetition.
3. Reading aloud.
4. Voluntary writing (figures to be tested especially) (p. 1119). Examination of written paraphasia (word confusion in writing).
5. Writing from dictation (figures to be tested especially).
6. Copying.
7. Speech comprehension.
8. Script comprehension (figures to be tested especially).
9. Counting syllables. (See p. 1106 et seq.)

It is usually better in complicated aphasias to test sensory speech first, since in judging the motor speech function one should know (especially in repetition and syllable counting) whether the tone images are formed or how much the patients understand.

(*b*) Test for Letters

1. Speaking the letters of the alphabet spontaneously with special attention to the quality of the pronunciation.
2. Repetition of letters.
3. Reading letters aloud.
4. Writing the alphabet spontaneously.
5. Writing letters from dictation.
6. Copying letters.
7. Recognition of spoken letters, *i. e.*, association of the sounds with the pictures of letters (picking out the corresponding printed letters).
8. Recognition of written or printed letters, *i. e.*, association of the letter pictures with the spoken letters (where the letters cannot be named, suggestive questions should be used in the test).

For the sake of localization one must ascertain whether the patient was right or left handed.

Since paralysis of the right arm is very commonly associated with aphasia, the patient's ability to write with the left hand should be tested (many aphasics produce mirror-writing). If the patient cannot write with the left hand, he should attempt to construct the words with letters such as are used in the ordinary game of anagrams.

If every case of aphasia is examined according to this plan, it is easy either to localize the aphasia at one or more definite points of the speech mechanism, or to determine that it is caused by an indefinite, *i. e.*, a functional or diffuse injury of the speech mechanism.

Finally, we should remember that these patients very rapidly become fatigued in performing the almost superhuman tasks that such an examination entails for them. Whenever this point is reached, it is better to discontinue the examination, for otherwise it becomes a useless torment, causing an aphasia which might be definitely localized to become so diffuse and indefinite as to lead one to false conclusions. This may readily be understood if we bear in mind that normal individuals may exhibit certain aphasic phenomena (misstatements, difficulty in naming, mild anarthric disturbances) during excessive cerebral fatigue. [Bonhoeffer[1] and Koch[2] have shown that the peculiar paraphasic utterances, so frequently seen in these states, are due to disturbances of the attention, and that they are most marked when the latter is

[1] Die Geisterstörungen der Gewohnheitstrinker, Gust. Fischer, Jena, 1901.
[2] Drug Deliria, Review of Neurology and Psychiatry, Feb., 1906.

at a low level. As it is well known that fatigue affects the attention very rapidly, and thereby increases the tendency to paraphasia even in normal individuals, we can easily see how a prolonged examination may intensify the aphasia and thus obscure the actual degree of speech disturbance.—Z.]

The symptom of "*perseveration*" (Neisser) may often be demonstrated in the examination of an aphasia. It consists in an inclination on the part of the patient to repeat the reaction when once it is found, even if he know he is saying or doing something incorrectly. There exists a certain amount of compulsion in this, which probably depends on the principle of the inclusion of the pathways. The patients themselves often become impatient.

VII. DISTURBANCES RELATED TO APHASIA; ASYMBOLIA; AMIMIA; APRAXIA; AMUSIA; PSYCHIC DEAFNESS; PSYCHIC BLINDNESS

Asymbolia is a condition of the mind in which the ability to make one's self understood by signs and gestures (as well as by speech) is impaired or lost. A differentiation may be made between active or motor and passive or sensory asymbolia, dependent upon whether pantomimic speech or the ability to understand it is affected.

Amimia is a disturbance or loss of the power of imitation, whether it be simply the mimicry associated with speech or the mimicry expressing psychic processes.

Apraxia (Liepman) is the inability to employ objects in the proper way, the patient taking a spoon or fork in his hand, for example, and being unable to use it correctly.

The disturbances just described are also characterized by the fact that they are not associated with actual motor paralysis, *i. e.*, with motor disturbances of the affected muscles for other muscular functions. The intimate relation between the functions above mentioned and the function of speech sufficiently explains the fact that these disturbances are found almost exclusively with aphasias, and that their localization is practically the same as that of aphasia. [A careful study of Marie's articles on aphasia will convince the reader that many of the examples of defective intelligence cited are in reality very good instances of apraxia.—Z.]

The loss of the ability to produce or comprehend music or musical sounds has been designated as **amusia.** From the definition, it will be seen that amusia may be either motor or sensory. Motor amusia is related to motor aphasia; it has a similar localization and is sometimes associated with it. Sensory amusia is related to sensory aphasia, with which it is not infrequently combined. Its presence is indicative of a lesion in the left temporal lobe. A special form of amusia, the loss of the ability to recognize the musical significance of notes or to sing or play from notes, has been designated as "note-blindness," and another form, in which the power to comprehend music has been abolished, has been rather inappropriately called "tone-deafness." The first corresponds to alexia both in its nature and probably also in its localization; the second corresponds to pure sensory aphasia.

Psychic deafness is a condition in which not only words, but all sounds, though heard and perceived as such, awaken no intelligent conception. This disturbance evidently includes sensory aphasia, and the relationship of the two conditions is shown by the fact that sensory aphasia or word-deafness is sometimes combined with psychic deafness or passes into the latter condition.

Psychic blindness[1] requires a more detailed description. By this term is meant that peculiar condition in which objects are seen but not recognized. In other words, in spite of retained optic perception (optic apperception), the association of optic impressions is no longer possible. It holds the same relation to blindness as does psychic deafness to deafness. Psychic blindness can be produced only by a lesion in the transcortical tracts of the visual apparatus, *i. e.*, by a lesion in the association fibers of the visual center (see p. 1095), and is associated with lesions in the occipital lobes. Psychic blindness, alexia, and optic aphasia are closely related conditions, having in common, an inability to estimate by association optic impressions; the anatomic lesions are correspondingly similar.

As the retinal impression of one eye, on account of the semidecussation of the optic nerve, affects both hemispheres, it is probable that the visual representations upon whose associations with other representations depends the recognition of objects, are, unlike speech or word representation, localized in both hemispheres.[2]

[1] See Lissauer, Arch. f. Psychiatrie, vol. xxi.

[2] This was established on p. 1115, under consideration of the localization of letter memory pictures; also that central vision is represented in both eyes.

This will explain the fact that complete psychic blindness is never observed in a unilateral lesion of the brain. If one hemisphere be completely preserved, visual perception and representation are not only pictured, but also associated; although a certain degree of psychic blindness has frequently been observed in the cases of left-sided lesion which cause alexia. (See p. 1117.) The following figure explains diagrammatically the occurrence of psychic blindness from bilateral lesions of the occipital lobes. It is supposed to represent a horizontal section of the brain: *a* the left, *b* the right retina; *c* the left, *d* the right visual center; *ad* and *bd* the fibers of the right, *ac* and *bc* those of the left optic tract; *ec* and *fd* represent diagrammatically examples of association fibers between the optic centers and other parts of the brain upon the same side. These are, of course, not single, but run in countless directions to all regions of the cortex not associated with vision, in fact, from each center of vision to both hemispheres. Now, according to the above, psychic blindness may arise from lesions of the bilateral association tracts (*ec* and *fd*)—for example, from lesions *g* and *h;* but it is highly improbable that in both posterior lobes only the association tracts should be affected in this way. As a matter of fact, heretofore it has been found that the fibers of the optic tract or even the visual center itself are

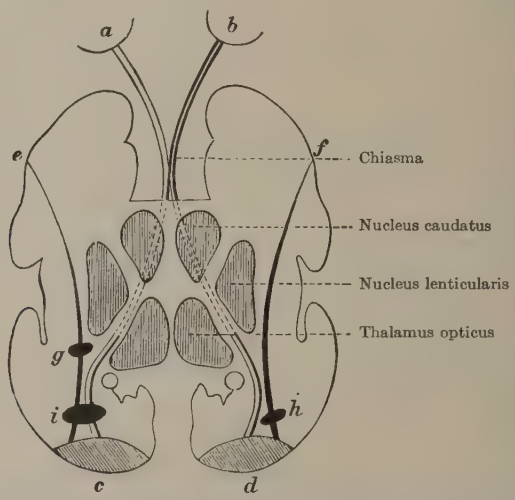


Fig. 444.—Diagram to explain the simultaneous occurrence of psychic blindness and hemiopia from a bilateral lesion in the occipital lobe. Horizontal cross-section of brain: *a*, Left retina; *b*, right retina;.*c*, left sight center; *d*, right sight center (see Fig. 424); *ad* and *bd*, fibers of the right, *ac* and *bc*, fibers of the left, optic tract; *g*, *h*, and *i*, lesions.

injured coincidentally with the association tracts upon the one side by a large lesion like *i;* whereas upon the other side a smaller lesion (*h*) may affect only the association tracts (and in contrast to the simplified figure those to both hemispheres) and not include the visual tracts or even the visual center.

A patient with such a bilateral lesion (*i* and *h*) presents clinically homonymous hemiopia, *i. e.*, he is absolutely blind to objects whose pictures fall upon the left retina. He perceives objects with the right retinal half, but he cannot recognize them, because the association of the right visual center with the remainder of the brain is interrupted. It need scarcely be emphasized that all the associations of optic representations need not be destroyed in every case of psychic blindness, but that in many cases only certain of them fail, while others are retained. Thus, it is conceivable that a patient can associate the optical representation of a rose with the word representation of a rose, but not with the representation of the smell of the rose. Such examples of partial psychic blindness are undoubtedly not so very rare in the psychoses. But we ordinarily speak of psychic blindness in the narrow sense of the word, or of a total psychic blindness, only when so many associations of the optical representations are lost that the conception of the latter (see p. 1103 et seq.) can no longer be elicited, *i. e.*, the object can no longer be recog-

nized. An interference with the association of the optic representation with the speech mechanism, which is a kind of partial psychic blindness, has been studied as a partial transcortical aphasia upon p. 1119, under the title of Optic Aphasia.

Complete psychic blindness frequently presents the clinical picture of mental confusion or insanity. Patients do not recognize objects at all, and behave in a most peculiar fashion. In certain characteristics they may behave like the blind, stumbling, for example, over objects which they may probably see but do not recognize. The condition is, therefore, often not very easy to diagnose, and in examining such a case the following plan may be adopted:

1. Examination of the apperception in order to differentiate from a simple visual disturbance or from blindness. To be tested are: refraction, visual field (determination of hemiopia), acuity of vision (this may be attempted with corrected refraction). Testing the visual acuity in psychic blindness naturally presents very serious obstacles, as the ordinary test objects, such as letters, etc., cannot be recognized. We are, therefore, usually obliged to make use of some artificial device, such as requiring the patient to name the number of black points upon a sheet of paper.

2. Examinations to determine whether visual representations exist. In this connection only the patient's statements about optical memory, etc., can furnish any information.

3. Examination of association of visual impressions. Recognition of objects by statement of the name or by demonstration of their use, reading (aloud and with comprehension), copying, drawing, voluntary reactions to optical irritation, power of orientation.

4. Examination of the association of visual representations. Drawing from memory, writing spontaneously, writing from dictation.

5. In differentiating psychic blindness from general confusion or insanity, it is necessary to determine whether the other perceptions, viz., those of hearing, smell, taste, as well as the sensory skin sensation, are properly associated, and to observe whether the patients deport themselves sensibly so far as their behavior toward visual sensations is concerned.

The diagnosis of actual psychic blindness is frequently very difficult, and is often impossible when complicated with marked diminution in vision, because conditions occur in all forms of diminished visual acuity which have this in common with real psychic blindness, that the significance of what is seen is disturbed merely because the visual impressions are not sharp enough.

Psychic blindness is not to be confused with *cortical blindness*. The latter affection is an actual blindness, a loss of the visual power, produced by lesions of the cortex, which, owing to the hemiopic distribution of the visual function in both hemispheres, must be bilateral.

VIII. SPINAL HEMIPLEGIA

Unilateral lesions of the spinal cord produce a symptom-complex which is known as "spinal hemiplegia," in the broadest sense of the word. This hemiplegia varies in character according to the location and extent of the lesion.

The *motor disturbances* appear in the extremity upon the same side as the lesion and in only the lower, or both the lower and the upper, extremities, according to the level of the lesion. The motor paralysis dependent upon an interruption of the long tracts, particularly of the pyramidal tract, is spastic in character, as in a complete transverse lesion of the cord, is associated with increased tendon reflexes, and is not accompanied by degenerative atrophy of the paralyzed muscles. If the lesion have a considerable vertical dimension, this spastic paralysis may be associated with a degenerative atrophic flaccid paralysis due to involvement of the nuclei in the anterior cornua. With an extensive vertical lesion in the cervical enlargement, for example, the spastic paralysis will be bounded above by a degenerative flaccid paralysis of the upper extremity; if the extensive vertical lesion be situated in the lumbar cord, the paralysis of the muscles supplied by the injured segments will be atrophic and relaxed. Should the lesion involve the entire length of the lumbar swelling, the spastic paralysis of the leg will be entirely replaced by a flaccid degenerative paralysis. In reference to the spastic components of the paralysis dependent upon the involvement of the long tracts, it may be said that the laws given for cerebral hemiplegia on p. 1088 et seq., in reference to the more or less marked involvement of the individual muscle groups, also obtain in spinal hemiplegia.

The *vasomotor* tracts are involved upon the side of the lesion, so that the extremity at first seems warmer than its fellow of the opposite side. This difference sub-

sequently becomes equalized by the decreased heat-production in the paralyzed muscles, and also by the disappearance of the vasomotor palsy as the result of the vicarious action of deeper centers. The paralyzed side may then even be colder to the touch than its opposite fellow.

The *sensory disturbances* in unilateral spinal lesions are of special interest and somewhat more complicated. We have just seen that the motor symptoms, corresponding to the uncrossed exit of the motor tracts from the spinal cord, occur only upon the same side as the lesion; but the sensory disturbances are partly bilateral,

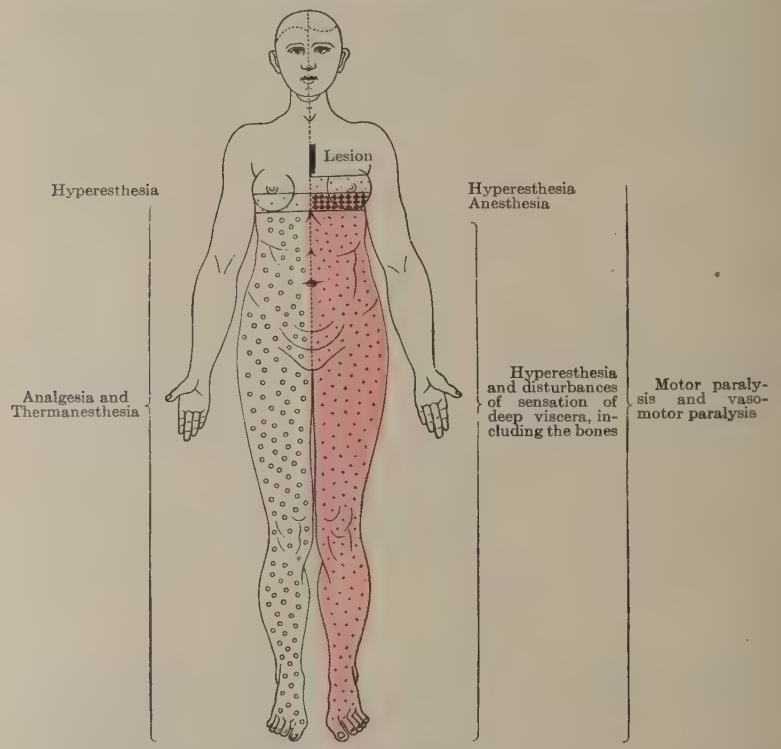


Fig. 445.—Spinal hemiplegia. Lesion upon the left side of the patient. Type 1: Motor and vasomotor paralysis. Varying degree of disturbance of sensation of the deep viscera (perception of position), including the bones.

Analgesia and thermanesthesia of the skin. Intact sensation to touch.

Cutaneous hyperesthesia to touch (also in the red shaded area).

Complete cutaneous anesthesia.

In the white areas there is neither motor nor vasomotor paralysis.

although most of them are present only upon the side opposite to the lesion. The observation of the sensory phenomena in such cases has resulted in the establishment of the three following types:[1]

Type 1 (Fig. 445). *Upon the same side as the lesion:* Cutaneous hyperesthesia of the skin to touch, bounded above by a zone of cutaneous anesthesia for all sensory qualities; above the latter area there is sometimes still another narrow zone of

[1] See Mann, Zeit. f. Nervenkrankh., 1896, vol. x, and Gowers' Handbook of Nervous Diseases.

hyperesthesia to touch. Disturbances of sensation of the deep viscera (disturbance of the perception of passive changes of the position of the extremities and of bone sensibility).

Upon the opposite side: Cutaneous analgesia and thermanesthesia, sometimes (though more rarely than upon the same side as the lesion) bounded above by a zone of cutaneous hyperesthesia to touch. Sensation to touch intact.

Type 2 (Fig. 446). As in Type 1, except that the analgesic and thermanesthetic regions upon the side opposite to the lesion also exhibit hyperesthesia or anesthesia to touch.

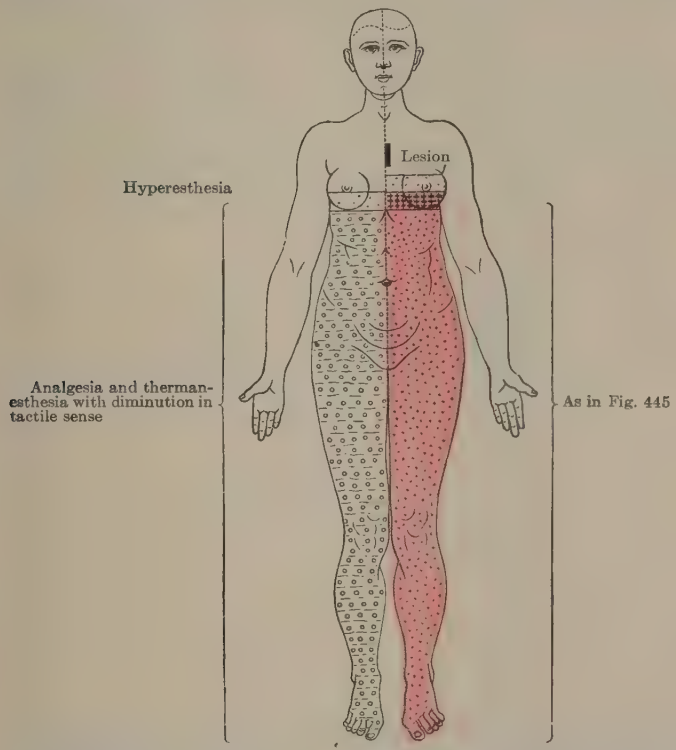


Fig. 446.—Spinal hemiplegia. Lesion upon the left side of the patient. Type 2: Motor and vasomotor paralysis. Varying degree of disturbance of sensation of the deep viscera (perception of position), including the bones.

Cutaneous hyperesthesia to touch (also in the red shaded area).

Complete anesthesia.

Diminished sensation to touch and abolished sensations of pain and temperature. Upon the white side there is neither motor nor vasomotor paralysis.

Type 3 (Fig. 447). As in Type 1, but, with the exception of the zones at the level of the lesion, there is no hyperesthesia to touch upon the side of the lesion; on both sides below the lesion or below the small zones of hyperalgesia there is hyperesthesia to touch (Gowers).

These different symptoms may be explained by the following assumptions: The majority of the fibers conducting the sensations of pain and temperature decussate immediately upon their entrance into the spinal cord and pass upward to the brain upon the other side of the median line. About half of the fibers conducting the sensation of touch decussate immediately and half remain upon the same side.

The fibers for the perception of passive movements of the extremities and for bone sensation run upward in the spinal cord without decussation. The uncrossed fibers probably pass upward in the posterior columns, while the crossed fibers, especially those for temperature and pain, after their decussation, run upward in the anterolateral columns. The decussation of the fibers in the latter group, if it occur at all (see above), takes place in the gray matter, since an impulse from the terminals of the collaterals in the posterior horn of one side is taken up by dendrites of the cells in

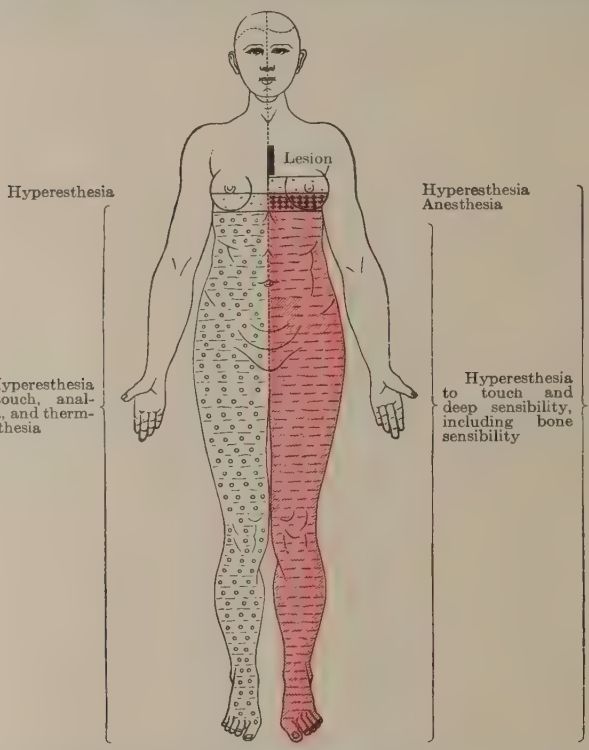


Fig. 447.—Spinal hemiplegia. Lesion upon the left side of the patient. Type 3: Motor and vasomotor paralysis. Varying degree of disturbance of sensation of the deep viscera (perception of position), including the bones.

Hyperesthesia to touch.

Complete anesthesia.

Diminished sensation to touch and abolished sensations of pain and temperature

Diminished sensation to touch (also in the red shaded area).
Upon the white side there is neither motor nor vasomotor paralysis.

the anterolateral column of the other side. (See Fig. 455.) It should be noted that, as the decussation never affects the entire fibers of the posterior roots, but always only their collaterals,[1] we might indicate the relation between the crossed and

[1] As is well known, every fiber of the posterior root immediately upon entering the spinal cord divides into an ascending and a descending branch, both of which give off transverse ramifications known as collaterals. These collaterals run approximately transversely in the cord, and send on the sensory impulses through their terminal arborizations.

uncrossed sensory fibers diagrammatically by representing the posterior root as consisting of a crossed and an uncrossed portion. This conception is of importance for the explanation of the hyperalgesia upon the side of the lesion. (See below.)

The most important of these assumptions are diagrammatically indicated in the accompanying illustration (Fig. 448). In order to render it more comprehensible, the sensory fibers for the perception of passive movements of the extremities and for bone sensation, as well as the motor and vasomotor fibers, have been omitted. This is more convenient because, as their course has been indicated by clinical observation, a disturbance of these tracts needs no special explanation. By the use of this diagram the differences between the sensory symptom-complexes of unilateral lesions may be readily understood.

The red lines represent the fibers for the conduction of the sensations of pain and temperature; although these sensations are not transmitted by the same fibers, they both pursue a similar course. The black lines represent the fibers for the conduction of the sensation of touch. It will be observed that each of these fibers, after its entrance into the spinal cord, divides into a crossed and a direct portion. The direct portions of the (red) fibers for the conduction of the impulses of pain and temperature are indicated by light lines, in order to give the impression that they are few in number and that they play an unimportant rôle in comparison with

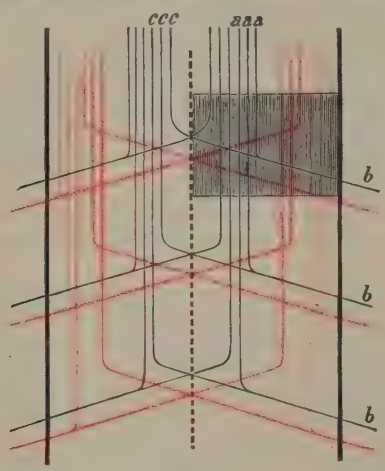


Fig. 448.—Diagram of the sensory fibers to explain the phenomena of spinal hemiplegia.

the much greater number of crossed fibers. The direct and the crossed portions of the (black) fibers for the sensation of touch are, on the contrary, indicated by exactly similar lines. For the sake of clearness, no attention has been paid to the topographic arrangement of the fibers in the cross-section of the spinal cord, nor to the composition of the crossed tracts from two neurons. The shaded area represents the substance of the spinal cord which is involved by a unilateral lesion.

With the aid of this figure the sensory phenomena of Type 1 (Fig. 445) may now be explained. The perceptions of passive motion of the extremities and of bone sensation will be disturbed upon the side of the lesion because these fibers (not indicated in Fig. 448) pass upward uncrossed in the spinal cord. We can also understand that a complete transverse section of one-half of the cord will be followed by an almost complete absence of the sensations of pain and temperature upon the opposite side below the lesion (due to involvement of the heavy red lines in Fig. 448). The direct fibers for these sensations (indicated by the light red lines) are so few in number that they are unable to produce symptoms upon the same side as the lesion, and are equally powerless to prevent a marked disturbance of the sensations for pain and temperature upon the opposite side. The figure also explains why in many cases there is no diminution of the sensation to touch below the lesion, with the exception of the zone corresponding to the involved segment, since the equal division of these fibers into crossed and uncrossed tracts is evidently sufficient to

maintain the normal sensory conditions. Many theories have been advanced to explain the hyperalgesia to touch which is usually observed upon the same side and below the lesion. The author believes that this symptom can be rendered intelligible by assuming that the crossed and direct tracts for tactile sensation are mutually complementary ramifications of the sensory roots. When the direct tracts *bbb aaa* are interrupted, the crossed tracts *bbb ccc* receive a nervous impulse of double intensity, and this intensity is sufficient to cause the impulse to radiate into the dendritic network of the gray matter and excite the tract for the sensation of pain. Upon the opposite side the crossed fibers for tactile sensation are involved, and this would be followed by hyperalgesia for analogous reasons were it not that the increased intensity of tactile sensations cannot be converted into pain on account of the interruption of the tract for its transmission. The anesthetic zone observed upon the side of the lesion is explained simply by the involvement of the spinal segment by the lesion, since all of the sensory root-fibers are interrupted. The hyperalgesic zone, sometimes observed above this anesthetic zone upon the same side as the lesion, and occasionally upon the opposite side, can hardly be explained otherwise than by the supposition that the roots in the vicinity of the lesion may easily be rendered hyperirritable by inflammatory hyperemia, possibly from the meninges.

The involvement of tactile sensation in the hemianesthesia opposite to the lesion in Type 2 (Fig. 446) is explained by assuming that in these cases the crossed fibers for tactile sensation preponderate greatly over the direct. Such individual peculiarities are frequently encountered in neuropathology.

The cases of Type 3 (Fig. 447), in which, instead of hyperalgesia to touch on the same side below the lesion, we have hyperesthesia on both sides below the lesion, are explained by the supposition that the excitability of the tract for tactile sensation is so diminished that the loss of one-half of its innervation results in a decrease of sensibility, and, since the fibers run to both sides, this symptom is bilateral. Hyperalgesia is not produced below and upon the same side as the lesion on account of the diminution of the sensory irritability.

It should also be noted that, according to the condition of irritability of the sensory tracts and according to the remote effects of the unilateral lesion upon the opposite side, the symptom-complex of spinal heimplegia is subject to still further variation.

IX. PATHOLOGIC GAITS AND POSTURES

In many diseases, and especially in nervous diseases, the way patients stand and walk shows something very characteristic, permitting a conclusion not only in regard to the type of the functional disturbance, but frequently even in regard to the anatomic nature of the disease. The following are the best-known pathologic gaits:

(*a*) **The Paraparetic or Paraplegic Gait.**—In paresis of both lower extremities. Both legs are brought forward slowly, dragging and trailing upon the floor.

(*b*) **The Hemiparetic or Hemiplegic Gait.**—In unilateral paralysis of the legs or hemiplegia. The affected leg drags after the other, or is first circumducted by a twisting movement of the pelvis and so brought forward. An explanation of this gait is to be found upon p. 1089 et seq. The predominance of the paralysis of the flexors is considered responsible for the hemiplegic disturbances of motility.

(*c*) **The Ataxic Gait.**—Characterized by the incoördinate ataxic nature of the movements. Sometimes the foot feels uncertainly for the ground, sometimes it is thrown outward at random or stamps, and again is lifted high from the ground, making the gait resemble that of a fowl. (See Ataxia, p. 962 et seq.)

(*d*) **The Spastic Gait.**—In spastic paresis of the lower extremities (spastic spinal paralysis, multiple sclerosis, etc.), the legs, being very slightly flexible, are put forward very stiffly. In putting the foot down the tendon reflexes (especially the Achilles-tendon reflex) are sometimes excited and the gait becomes characteristically jumping. The

difficulty in the spastic gait depends at one time more upon the stiffness of the knee-joints, at another more upon the knees being pressed together by the forcible action of the adductors.

(*e*) **The Spastic Paretic Gait.**—Combination of *a* and *c*.

(*f*) **The Gait of Hip-joint Disease.**—This is characterized by a rigidity of the hip-joint, so that the pelvis is largely responsible for any forward motion of the limb. Under some conditions the gait in hysteric coxalgia may be identical.

(*g*) The **gait in sciatica** may resemble that in hip-joint disease. The patient favors the affected leg by fixing it to the pelvis, almost as regularly as in hip-joint disease. In so-called sciatic scoliosis the vertebral column is curved while the patient is walking or standing. There are usually two characteristic curves: the lower curve is convex, the upper concave toward the affected side. The trunk is, therefore, as a rule, bent toward the healthy side (heterologous sciatic scoliosis), although the curves may be reversed (homologous sciatic scoliosis).

Attempts have been made to explain these differences in sciatic scoliosis, but it seems quite plain that no explanation is possible for them all. Albert described heterologous sciatic scoliosis, but did not venture an explanation. Lorenz assumes that this form of scoliosis is brought about simply by shifting the center of gravity to the healthy leg. Kocher explains it by an associated neuralgic affection of the sensory nerves supplying the territory of those muscles which hold the trunk straight. When the contraction of these muscles results in pain, it is no longer attempted. The spinal column, therefore, bends, its direction depending upon what nerves are thus affected.

(*h*) **The Choreic Gait.**—In chorea. (See Choreic Movements, p. 959.)

(*i*) **The Staggering Gait.**—In affections which are associated with vertigo (see Cerebellar Ataxia, p. 965, and Vertigo, p. 1092) and disturbances of equilibrium (drunkenness, cerebellar tumor, paralyses of the eye muscles, diseases of the internal or middle ear, lead encephalopathy).

(*k*) **The Gait of Propulsion and Retropulsion.**—In affections with stiffness and weakness of the muscles, especially in *paralysis agitans*. This gait is peculiar in that patients once started forward or backward are not able to stop quickly, but must go on a little farther in the direction in which they are headed, because they cannot quickly enough correct the position of the center of gravity which has been shifted in the direction of their motion. Although especially frequent in paralysis agitans, it is not really specific, as is sometimes thought, for one often notices the same peculiarity in pedestrians who have been tired by a long tramp.

The *attitude* or mode of standing is very characteristic in many of the affections cited above. In *hip-joint disease* and in *unilateral leg paralysis* the patient supports himself entirely upon the healthy leg.

In *sciatica* the scoliotic appearances described above are very prominent. In *paralysis agitans* the position of the trunk, bent over forward, with slightly flexed knees and elbow-joints, is highly characteristic. (See the picture in Strümpell's Lehrbuch der Pathologie.) *Romberg's symptom* consists of more or less noticeable swaying in patients who stand with closed eyes (in severe cases even with open eyes). It occurs in anesthesia of the lower extremities, also in ataxia with or without anesthesia (especially in tabes), in affections of the cerebellum, and in

some other affections [alcoholic multiple neuritis—Z.] which lead to a staggering gait. (See above.) The sign depends upon a disturbance of the equilibrium.

X. SPECIAL POINTS IN REFERENCE TO THE EXAMINATION OF THE SPINAL NERVOUS SYSTEM

I. PLANS FOR THE EXAMINATION OF MUSCLE ATROPHIES AND PERIPHERAL MOTOR PARALYSIS[1]

Upper Extremities

(For motor points, see p. 1013 et seq.)

Shoulder-blade Movements

1. *Elevation of the Shoulder-blade.*
   - Middle portion of the trapezius (spinal accessory).
   - Rhomboids (branch from fifth cervical).
   - Levator anguli scapulæ (second to third cervical and branch from fifth cervical).
   - Superior portion of the pectoralis major (anterior thoracic from fifth and sixth cervical).
2. *Depression of the Shoulder-blade.*
   - Pectoralis minor (anterior thoracic).
   - Inferior portion of the latissimus dorsi (subscapular).
   - Inferior portion of the pectoralis major (anterior thoracic).
3. *Adduction of the Shoulder-blade.*
   - Inferior portion of the trapezius (spinal accessory).
   - Superior portion of the latissimus dorsi (subscapular).
   - Rhomboids. (Branch from fifth cervical.)
4. *Abduction of the Shoulder-blade.*
   - Superior third of the pectoralis major (anterior thoracic).
   - Serratus magnus (posterior thoracic from sixth, seventh, and eighth cervical nerves).

Shoulder-joint Movements

1. *Elevation of the Upper Arm.*
   - (*a*) To the side:
     - Up to the horizontal: deltoid (circumflex).
     - Up to the vertical: deltoid and serratus magnus (posterior thoracic).
       - With straining, the upper part of the trapezius in addition (spinal accessory).
   - (*b*) Forward:
     - Anterior portion of the deltoid (circumflex).
     - Coracobrachialis (musculocutaneous).
     - Biceps (musculocutaneous).
       - In elevation to the vertical, the serratus magnus also aids.
   - (*c*) Backward:
     - Posterior portion of the deltoid (circumflex).

[1] The anatomic statements in these schemes have been collected from Scheube and Duchenne, and then compared with Gegenbauer's Anatomy (fourth edition, 1890). For the sake of simplicity, the origin of a nerve from its motor root is stated in the plan only where the nerve is mentioned for the first time. In this way it is easy enough to find the root origin of a certain nerve for a certain muscle by searching for the name of this nerve in the first place it is mentioned in the scheme. For those nerves whose origin is not stated in the scheme, the reader should consult the diagrams of the plexuses for the extremities, pp. 1158, 1159, and Kocher's plates of the spinal motor segmental innervation (Figs. 462 and 463). Further clinical experience is necessary to clear up individual points and deficiencies still under contention.

2. *Depression of the Upper Arm.*
   The united adductors of the upper arm.
3. *Adduction of the Upper Arm.*
   Pectoralis major (anterior thoracic from fifth and sixth cervical).
   Latissimus dorsi and teres major (subscapular).
   Infraspinatus (suprascapular from fifth and sixth cervical).
   Teres minor (circumflex).
4. *Inward Rotation of the Upper Arm.*
   Subscapularis (subscapular).
   Teres major (subscapular).
5. *Outward Rotation of the Upper Arm.*
   Infraspinatus (suprascapular).
   Teres minor (circumflex).

Elbow-joint Movements

1. *Flexion of the Forearm.*
   Biceps [flexor and supinator] (musculocutaneous).
   Brachialis anticus (musculocutaneous).
   Supinator longus [supinates or pronates according to the position; it is, however, chiefly a flexor in the median position] (musculospiral).
2. *Extension of the Forearm.*
   Triceps (musculospiral).
3. *Supination of the Forearm.*
   Supinator brevis (musculospiral).
   Supinator longus (see Flexion).
4. *Pronation of the Forearm.*
   Pronator quadratus (median).
   Pronator teres [pronation and flexion] (median).
   Supinator longus [in an extreme position of supination] (musculospiral).

Wrist Movements

1. *Flexion of the Hand.*
   Flexor carpi radialis [flexion to the radial side] (median).
   Flexor carpi ulnaris [flexion to the ulnar side] (ulnar).
   Palmaris longus (ulnar).
2. *Extension of the Hand.*
   Extensor carpi radialis longior and brevior [extension to the radial side] (musculospiral).
   Extensor carpi ulnaris [extension to the ulnar side] (musculospiral).
3. *Abduction (Radial Flexion) of the Hand.*
   Flexor carpi radialis and extensor carpi radialis longior and brevior (median and musculospiral).
4. *Adduction (Ulnar Flexion) of the Hand.*
   Extensor carpi ulnaris and flexor carpi ulnaris (musculospiral and ulnar).

Finger Movements

1. *Flexion of the Fingers.*
   Flexor digitorum sublimis [flexing the second phalanx] (median).
   Flexor digitorum profundus [flexing the finger from the distal phalanx] (median and ulnar. The former supplies the radial sides; the latter, the ulnar sides of the several fingers).
   The interossei and lumbricales (flexing the proximal phalanx and extending the two distal phalanges). Nerve-supply principally the ulnar; in the innervation of the lumbricales, the ulnar nerve is aided by the median nerve to the extent that the latter is distributed to the two radial and a portion of the next lumbrical, while the ulnar supplies the rest.
2. *Extension of the Fingers.*
   Extensor digitorum communis, extensor indicis, extensor minimi digiti [extending the proximal phalanx] (musculospiral).
   Interossei and lumbricales [extending the two distal phalanges] (ulnar and median; see above).

3. *Adduction of the Fingers.*
   Palmar interossei [flexing the proximal phalanx simultaneously] (ulnar).
4. *Abduction of the Fingers.*
   Dorsal interossei [flexing the proximal phalanx simultaneously] (ulnar).

Thumb Movements

1. *Flexion of the Thumb.*
   Flexor longus pollicis [flexing the distal phalanx] (median).
   Flexor brevis pollicis [flexing the proximal phalanx] (median).
2. *Extension of the Thumb.*
   Extensor brevis pollicis (musculospiral).
   Extensor longus pollicis (musculospiral).
3. *Abduction of the Thumb.*
   Abductor longus pollicis (musculospiral).
   Abductor brevis pollicis [more opponens than abductor] (median).
4. *Adduction of the Thumb.*
   Adductor pollicis (ulnar).
5. *Opposition of the Thumb.*
   Opponens pollicis (median).
   Abductor brevis pollicis [more opponens than abductor] (median).

Little-finger Movements

1. *Flexion of the Little Finger.*
   Flexor digitorum communis profundus and sublimis (median and ulnar).
   Flexor brevis minimi digiti (ulnar).
2. *Extension of the Little Finger.*
   Extensor minimi digiti proprius (musculospiral).
3. *Abduction of the Little Finger.*
   Abductor minimi digiti (ulnar).
4. *Opposition of the Little Finger.*
   Opponens minimi digiti (ulnar).

Lower Extremities

(For motor points, see p. 1013 et seq.)

Hip-joint Movements

1. *Elevation of the Thigh.*
   Iliopsoas [outward rotation simultaneously] (lumbar plexus).
   Rectus femoris. } (crural from the first to fourth lumbar).
   Sartorius. }
2. *Depression of the Thigh.*
   Gluteus maximus [outward rotation simultaneously] (gluteal inferior from ischiadic plexus).
   Biceps } (ischiadic, fourth lumbar to third sacral) [at the same time flexing the leg, but only with extension of the thigh, not in walking—Wernicke-Mann. (See p. 1088.)]
   Semitendinosus }
   Semimembranosus }
3. *Inward Rotation of the Thigh.*
   Gluteus medius et minimus (gluteal superior from ischiadic plexus).
4. *Outward Rotation of the Thigh.*
   Quadratus femoris } (sciatic).
   Obturator internus and gemelli }
   Obturator externus (obturator from second to fourth lumbar).
   Pyriformis (ischiadic plexus).
   Iliopsoas (lumbar plexus).
   Gluteus maximus (gluteal inferior from ischiadic plexus).
5. *Adduction of the Thigh.*
   Adductors [simultaneous outward rotation] (obturator).
   Pectineus [simultaneous flexion] (crural and obturator).
   Gracilis (obturator).
6. *Abduction of the Thigh.*
   Gluteus medius et minimus (gluteal superior).

Knee-joint Movements

1. *Flexion of the Leg.*
   - Sartorius [simultaneous inward rotation of the flexed leg] (crural).
   - Gracilis [simultaneous inward rotation] (obturator).
   - } Principal flexor (shortener of the leg) in walking—Wernicke-Mann. (See p. 1088.)
   - Semitendinosus } [simultaneous inward rotation] (sciatic).
   - Semimembranosus } [simultaneous inward rotation] (sciatic).
   - Biceps [simultaneous outward rotation] (sciatic).
   - } Not as flexor of the leg, but as extensor of the thigh in walking (elongator of the leg—Wernicke-Mann. (See p. 1088.)
   - Popliteus [simultaneous inward rotation] (internal popliteal from sciatic).
2. *Extension of the Leg.*
   - Quadriceps (anterior crural).
3. *Inward Rotation of the Leg.*
   - Popliteus (internal popliteal).
   - Sartorius (anterior crural).
   - Gracilis (obturator).
   - Semitendinosus } (sciatic).
   - Semimembranosus } (sciatic).
4. *Outward Rotation of the Leg.*
   - Biceps (sciatic).

Foot-joint Movements (Sciatic)

1. *Dorsal Flexion of the Foot.*
   - Tibialis anticus [elevating at the same time the inner edge of the foot] (anterior tibial nerve from sciatic).
   - Extensor digitorum communis longus (simultaneous abduction).
2. *Extension (Plantar Flexion) of the Foot.*
   - Gastrocnemii } (internal popliteal from sciatic).
   - Soleus } (internal popliteal from sciatic).
   - Peroneus longus [simultaneous abductor and elevator of the outer edge of the foot] (musculocutaneous nerve from sciatic).
3. *Adduction of the Foot.*
   - Tibialis posticus [simultaneous raising of the inner edge of the foot and plantar flexion of the foot] (posterior tibial nerve).
   - Tibialis anticus [simultaneous dorsal flexion of the foot and raising of the inner edge of the foot] (anterior tibial nerve).
4. *Abduction of the Foot.*
   - Peroneus longus [simultaneous plantar flexion with elevation of the outer edge of the foot] (musculocutaneous).
   - Peroneus brevis [pure (?) abductor with elevation of the outer edge of the foot] (musculocutaneous).
   - Extensor digitorum communis longus (anterior tibial).
5. *Elevation of the Inner Edge of the Foot.*
   - Tibialis anticus [simultaneous dorsal flexion and adduction] (anterior tibial).
   - Tibialis posticus [simultaneous adduction and plantar flexion] (internal popliteal).
6. *Elevation of the Outer Edge of the Foot.*
   - Peroneus longus and peroneus brevis (musculocutaneous).
   - Peroneus tertius (anterior tibial).

Toe Movements (Sciatic)

1. *Flexion of the Toes.*
   - Flexor digitorum communis longus and brevis [second and third phalanges] (tibial).
   - Interossei and lumbricales [first phalanx] (tibial).
2. *Extension of the Toes.*
   - Extensor digitorum communis longus and brevis (anterior tibial).

3. *Adduction of the Toes.*
   Interossei plantares (tibial).
4. *Abduction of the Toes.*
   Interossei dorsales (tibial).

Great-toe Movements (Sciatic)

1. *Flexion of the Great Toe.*
   Flexor hallucis longus [second phalanx] (tibial).
   Flexor hallucis brevis [first phalanx] (tibial).
2. *Extension of the Great Toe.*
   Extensor hallucis longus [second phalanx] (anterior tibial).
   Extensor hallucis brevis [first phalanx] (anterior tibial).
3. *Adduction of the Great Toe.*
   Adductor hallucis. } (tibial).
   Inner belly of the flexor hallucis brevis } (tibial).
4. *Abduction of the Great Toe.*
   Abductor hallucis } (tibial).
   Outer belly of the flexor hallucis brevis } (tibial).

Little-toe Movements (Tibial)

1. *Flexion of the Little Toe.*
   Flexor digiti quinti (tibial).
2. *Abduction of the Little Toe.*
   Abductor digiti quinti (tibial).
3. *Opposition of the Little Toe.*
   Opponens digiti quinti (tibial).

2. THE PERIPHERAL DISTRIBUTION OF THE SENSORY CUTANEOUS NERVES

For the localization of peripheral sensory disturbances consult Figs. 449–454.

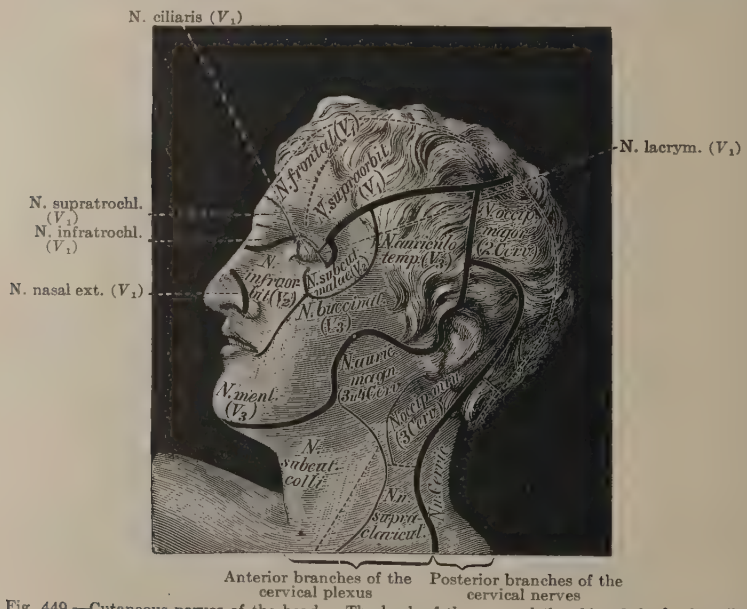


Fig. 449.—Cutaneous nerves of the head. The back of the ear and the skin of the back wall of the external auditory meatus are supplied by the auricularis vagi.

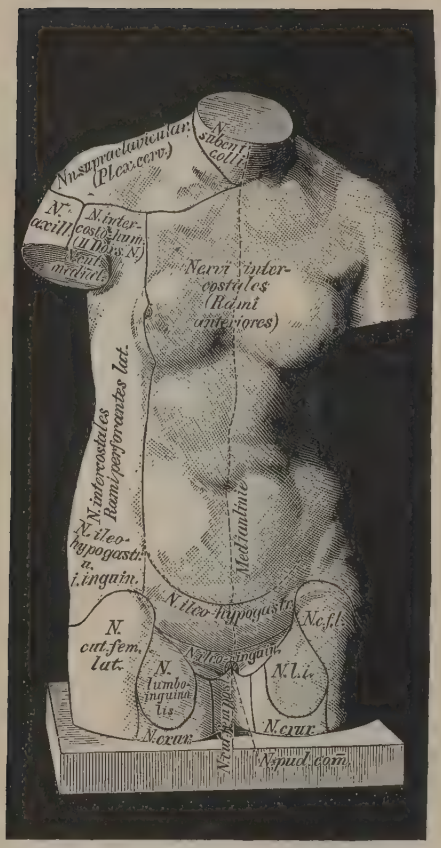


Fig. 450.—Cutaneous nerves of the anterior surface of the trunk. (See also Figs. 457–459.)

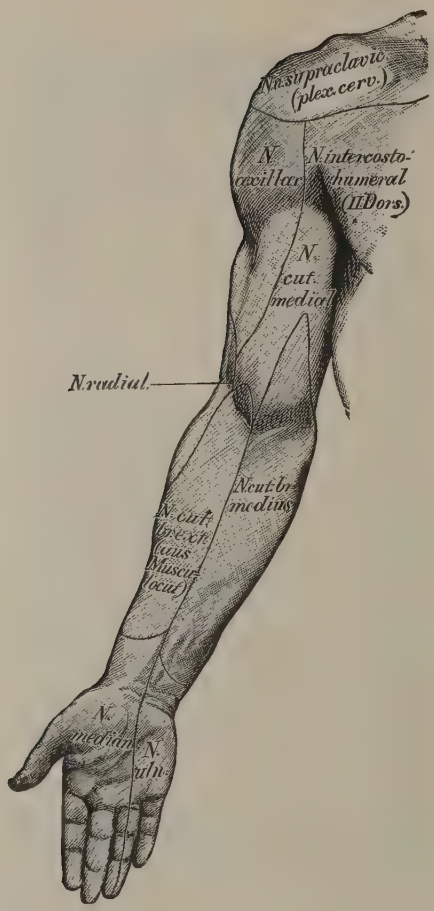


Fig. 451.—Cutaneous nerves of the flexor surface of the upper extremity. (See also Figs. 457–459.

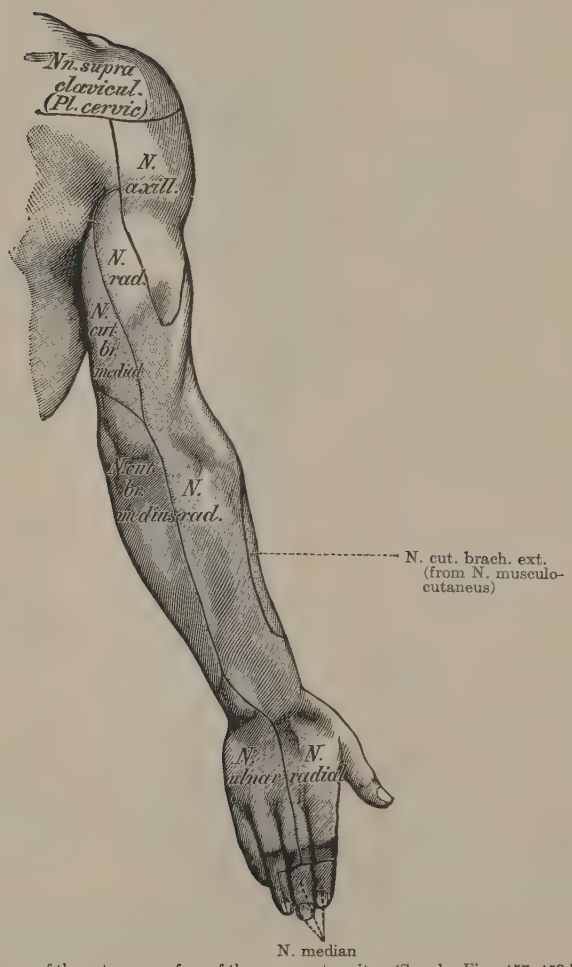


Fig. 452.—Cutaneous nerves of the extensor surface of the upper extremity. (See also Figs. 457–459.)

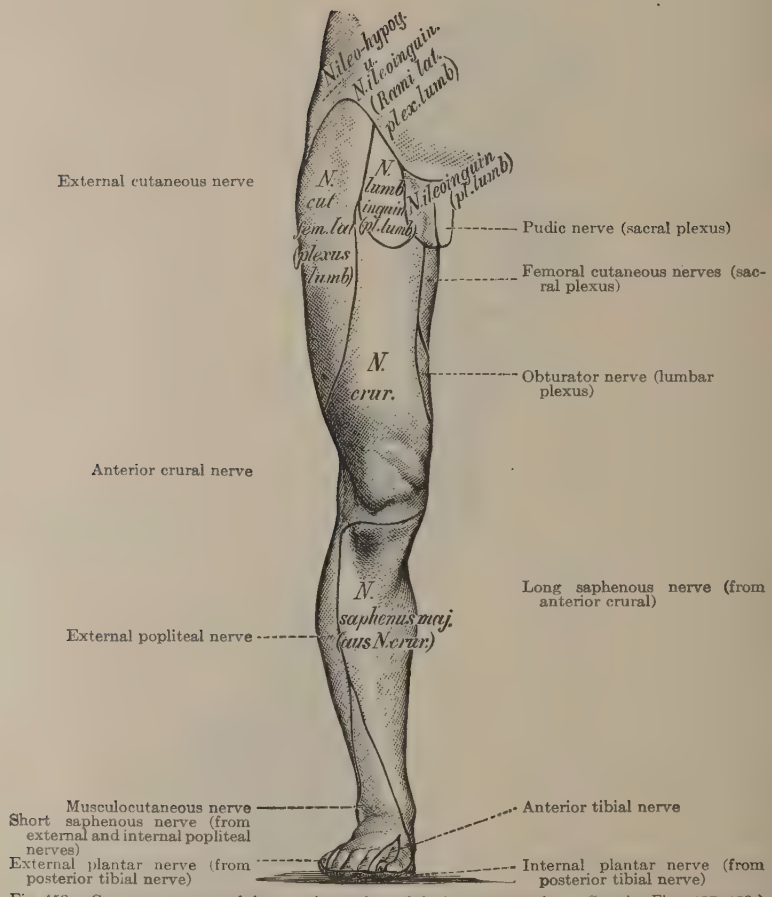


Fig. 453.—Cutaneous nerves of the anterior surface of the lower extremity. (See also Figs. 457–459.)

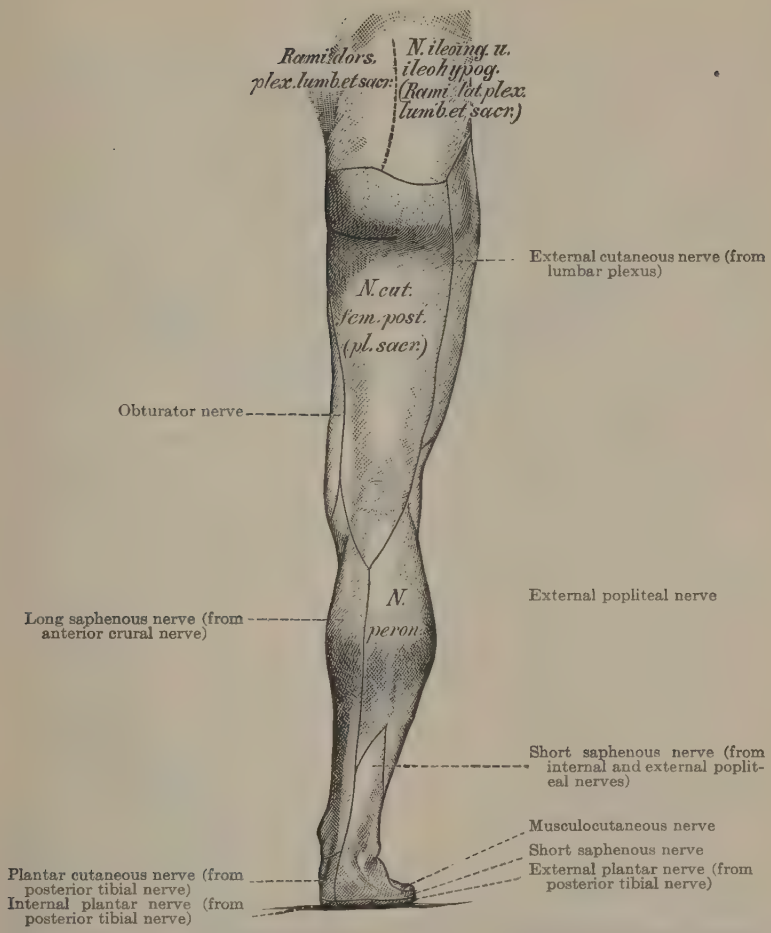


Fig. 454.—Cutaneous nerves of the posterior surface of the lower extremity. (See also Figs. 457–459.)

3. SPINAL LOCALIZATIONS

(*a*) Cross-section Localization of the Spinal Cord

In regard to this point the reader is referred to the text-books upon anatomy and physiology, which discuss the anatomic significance and the physiologic functions of the individual areas of the cross-section. We must be content here with inserting the two plates taken from Edinger and Obersteiner for orientation of the sensory tracts.

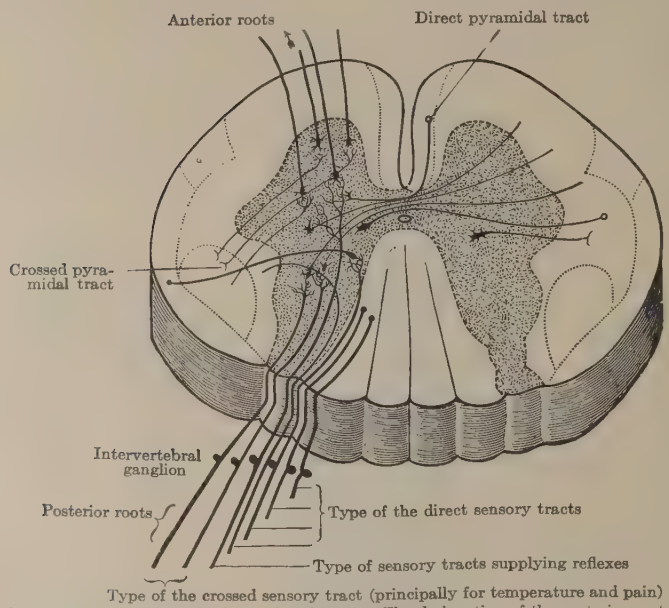


Fig. 455.—Cross-section of the cord (Edinger). The designation of the posterior roots not according to Edinger.

B, Burdach's column; *Ca*, anterior commissure; *Coa*, anterior cornu; *Cop*, posterior cornu; *GS*, column of Goll; *GSZ*, mixed lateral tract; *Ha*, postero-external field; *iS*, intermediate lateral tract; *KS*, direct cerebellar tract; *L*, Lissauer's marginal zone; *PyS*, lateral pyramidal tract; *m*, marginal zone; *PyV*, anterior pyramidal tract; *R*, substantia gelatinosa Rolandi; *Ra*, anterior roots; *SC*, Schultze's comma; *SG*, lateral boundary zone; *Sgc*, substantia gelatinosa centralis; *VG*, anterior ground bundle; *vH*, central substance behind the columns; *vm*, fasciculus sulcomarginalis; *Rp*, and *W*, posterior roots.

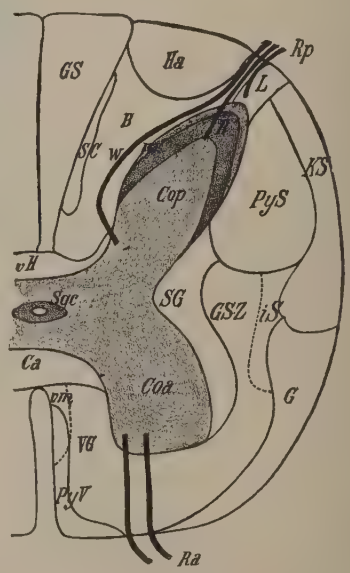


Fig. 456.—Cross-section of the cervical cord (after Obersteiner).

(b) Segmental Localization of the Spinal Cord—Longitudinal Localization

Recent Views

Segmental Localization of Cutaneous Sensibility.—The behavior of the cutaneous sensibility in lesions of separate sensory roots, *i. e.*, of separate segments of the spinal cord, has been very minutely studied recently by Sherrington,[1] Thoburn,[2] and Kocher.[3] Sherrington has shown experimentally that individual sensory roots, *i. e.*, segments of the dorsal cord, supply a circular girdle-shaped area of the skin upon the trunk, and that the individual segments overlap each other in both directions. Hence, the upper boundary of the disturbance of sensibility, in cross-lesions of the spinal cord, does not follow the descending direction of the ribs, but presents a girdle-shaped line perpendicular to the body axis. (See Figs. 457 to 459.) On account of the overlapping of the separate zones of sensibility, we find that in transverse lesions of the spinal cord a zone of relatively disturbed sensibility can always be distinguished above, between the boundary of the absolute loss of sensibility and the higher zone of hyperesthesia. (See p. 1126.) This zone of relatively disturbed sensibility corresponds to the area which is supplied also by the segment lying above the lesion, and which is deprived of the lower part of its double innervation. As is shown by the figure, the rules for the segmentary arrangements of disturbance of sensibility do not hold good for the extremities or the neck and head. However, if the arms be horizontally abducted, these rules still apply (Figs. 457 to 459).

In almost complete conformity with the experiments of Sherrington and with the clinical observations of Thoburn, Kocher, from minute investigation of traumatic lesions of the spinal cord, has represented in Fig. 457 the cutaneous areas corresponding to the separate spinal cord segments, *i. e.*, the sensory roots. We should supplement this figure by including the overlapping of the zones, as determined by Sherrington. In Fig. 457 the boundary between each segment and the one next below corresponds, according to Kocher, to the upper limits of the absolute disturbance of sensibility which he found in individual cases of transverse lesions of the spinal cord, *i. e.*, to the lower limits of the innervation area of the upper segment. Therefore, all these boundaries should be understood as representing the lower limits of the upper zone, *e. g.*, the boundary between the seventh and eighth dorsal zones corresponds to the lower boundary of the seventh zone, *i. e.*, to a level to which the seventh zone still sends its prolongations in lesions of the eighth segment, as a result of the double innervation; but the upper boundary of the eighth innervation area should be sought somewhat farther upward. The upper sensibility zone must, therefore, be understood to overlap the lower, like shingles on a roof, although in the figure only the uncovered parts are represented. Figs. 458 and 459 give the same representation (Seiffer and Edinger.)

The relation of the plane of the sensibility zones of the skin, *i. e.*,

[1] Philosophical Transactions of the Royal Society, London, 1893, vol. clxxxiv.

[2] A Contribution to the Surgery of the Spinal Cord, London, 1889, Griffin & Co.; also Brain, 1893 and 1894.

[3] Die Verletzungen der Wirbelsäule, zugleich als Beitrag zur Physiologie des menschlichen Rückenmarks, Mittheilung aus den Grenzgebeiten der Medicin und Chirurgie, vol. i, part 4.

of the anesthesia in lesions of the sensory roots or *focal* lesions of the cord, to the plane of the corresponding spinal cord segments, spinal root outlets, and vertebræ is of the greatest importance. Fig. 460, according to Gowers, and the following pages demonstrate plainly

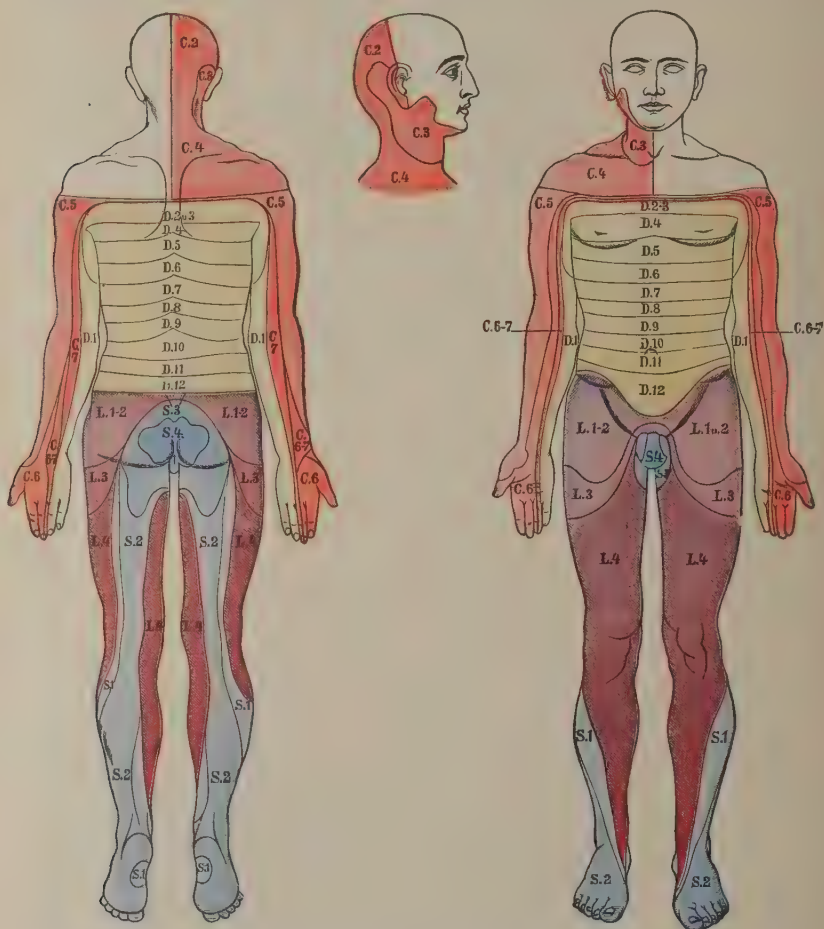


Fig. 457.—The sensory innervation of the body by the spinal segments, according to Kocher. The lines represent the lower border of the upper segments.
Red: Cervical segments.
Brown: Dorsal "
Violet: Lumbar "
Blue: Sacral "
} The intensity of the color depends upon the level of the segment.
C_2, D_2, L_2, S_2, etc. = Second cervical, dorsal, lumbar, sacral segment, etc.

enough that the injured spinal cord segment, the place of exit of the corresponding sensory root, or the vertebra corresponding numerically to the injured segment, and, finally, the cutaneous sensibility border do not lie in a horizontal plane, but that the cutaneous sensibility is

displaced well downward in relation to the vertebra or the exit of the nerve, and this again in relation to the segment of the cord. In the operative treatment of certain spinal cord affections, a neglect of this peculiarity has occasioned many unfortunate results. The plainest rules for use in such conditions have been recently formulated by Kocher,

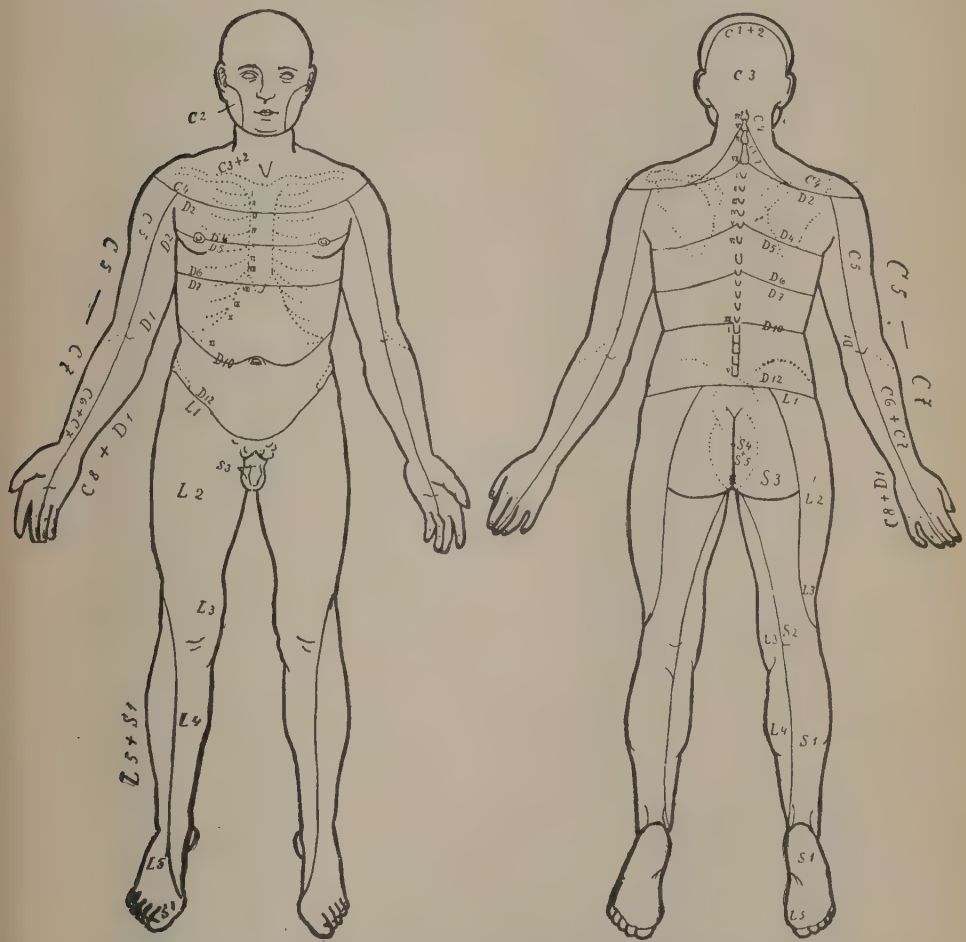


Fig. 458.—Sensory innervation of the spinal segments, according to Seiffer. The lines represent in this instance the lower border of the upper segments. The illustrations of Head's zones of hyperalgesia and irradiation (Figs. 381 and 382) correspond practically to these.

agreeing with Gowers' representation (Fig. 460). They will be given later.

One reason for such caudal displacement of the limits of cutaneous sensibility, as compared with the affected segment, depends upon the fact that the spinal cord (Fig. 460) is so much shorter than the vertebral

column that the nerve-roots within the vertebral canal must take a descending course. As a result (see Fig. 461) each segment up to the fourth or fifth upper dorsal vertebra is situated at the level of the next higher vertebra. Thus, the first dorsal root arises from its segment in

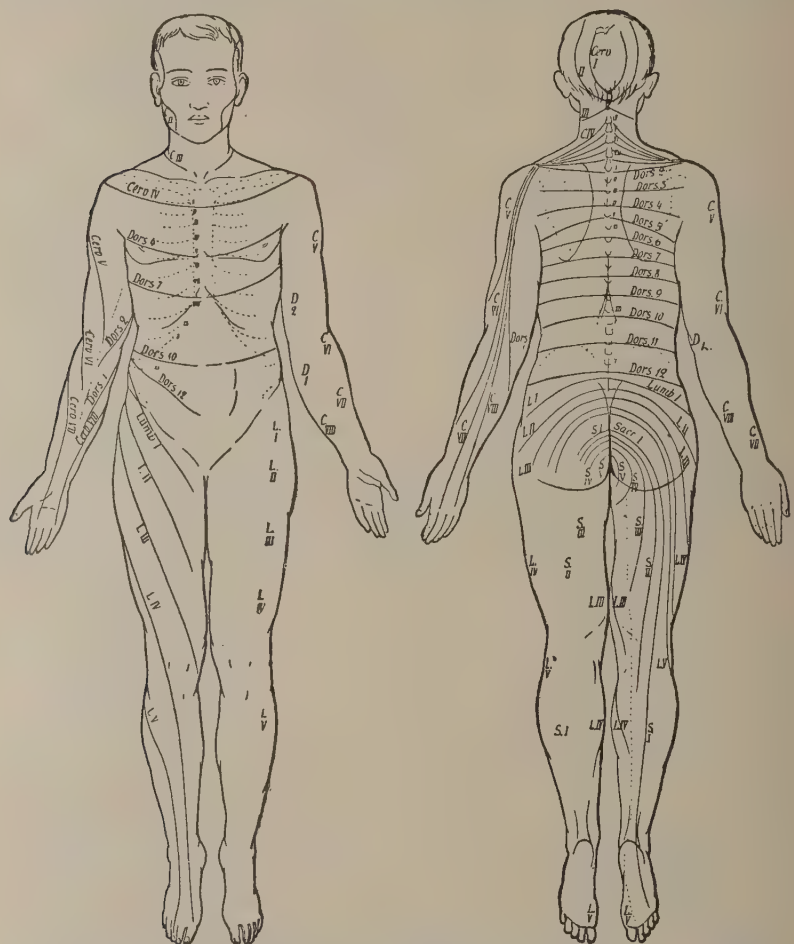


Fig. 459.—Sensory cutaneous innervations, according to the spinal segments, after Edinger. These lines do not represent the sensory segmental boundaries, but merely the axial directions of the segmental areas. This avoids the individual variations of the boundaries and the difficulties resulting from the overlapping of the segments.

the spinal cord behind the seventh cervical vertebra, the sixth dorsal root behind the fifth dorsal vertebra, etc. From the fourth or fifth vertebra downward the segments lie still higher in relation to the corresponding vertebra, so that the eighth dorsal segment lies behind the *upper* part of the seventh dorsal vertebra; the ninth segment, behind

the cartilage between the seventh and the eighth vertebra; the tenth segment, behind the lower part of the eighth; the eleventh, behind the ninth; the twelfth, behind the tenth vertebra. Thus, in the upper half of the dorsal column the difference of level between the segment and the corresponding vertebra is equal to the height of one vertebra; whereas in the lower dorsal column it approaches more and more the height of two vertebræ.

This variation of level between the segment and the corresponding vertebra naturally shows at the same time the difference in height between the segment and the exit of the corresponding roots.

Now, the upper boundaries of the absolute sensibility disturbance which correspond to a lesion of a certain nerve-root, *i. e.*, of its corresponding segment, are again lower than the point of exit of the nerve-root, because the intercostal nerves take a still further descending course to reach the skin, and because the unaffected root which lies above overlaps about one finger's breadth the area supplied by the affected root. In consequence of this in lesions of a sensory root, or in transverse lesions of the dorsal cord, the limits of sensibility (upper border of absolute anesthesia) are in the upper dorsal region, at the level of about three, in the lower dorsal from four to five, vertebræ below the points of exit of the affected roots, *i. e.*, the uppermost segments affected. Since the spinal cord segments in the upper dorsal column are situated at the distance of about one and in the lower dorsal two vertebræ above the exit of the corresponding nerve-root, the affected segment in cross-lesions of the upper part of the dorsal cord is situated about four (3 + 1),

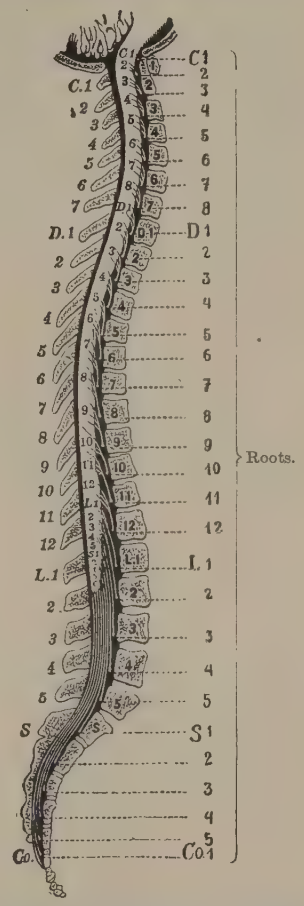


Fig. 460.—Longitudinal section of the spine, representing the topographic relations between the spinal segments, the outgoing roots, and vertebræ (after Gowers). It will be seen that only in the lumbar region are the spinous processes on the same level as the body of the vertebra; in the cervical region and the first two thoracic vertebræ the spinous processes correspond to the lower edge of the vertebral body; in the remainder to the upper edge of the next lower. Each cervical spinous process lies on the same level with the lowest root-fibers of the next numerically succeeding nerve. The spinal processes of the third to the tenth thoracic vertebræ correspond to the second numerically succeeding root. The eleventh process corresponds to the first and second lumbar roots, the twelfth to the third, fourth, and fifth. The first lumbar process corresponds to the second and third sacral roots; the end of the cord lies opposite the upper part of the second lumbar process.

and of the lower part of the dorsal cord from six to seven, spinous processes above the upper boundaries of absolute anesthesia.

These relations are represented diagrammatically in Fig. 461.

This diagram corresponds with the rules empirically established by Kocher, viz., that in cross-lesions of the dorsal cord (*i. e.*, in lesions of its sensory roots) the upper boundaries of absolute sensibility disturbance correspond to the deepest (caudal), and to the most anterior (ventral) point (for the upper ribs) of the intercostal space in which the intercostal nerve belonging to the affected root runs. From this level the limits of sensibility are horizontal, *i. e.*, perpendicular to the vertebral column, and not oblique, like the ribs. For those roots whose inter-

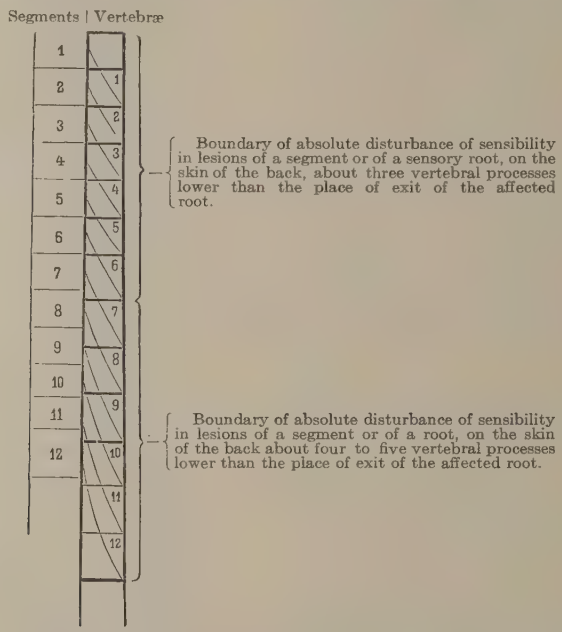


Fig. 461.—Diagram of the level of the dorsal segments in relation to the dorsal vertebræ and to the corresponding boundaries of the zones of insensibility on the back. Drawn from Kocher's rules. The oblique lines represent the emerging roots.

costal spaces do not reach the sternum, we must determine the boundaries anteriorly, corresponding to the supply of the abdominal wall, by following the intercostal nerve downward in a curve convex outward, *e. g.*, the boundaries corresponding to the twelfth intercostal nerve will reach down to the symphysis. (See Figs. 357–359, p. 1144 et seq.) In reality, Kocher's rules hold good even here, because the borders run practically horizontally backward from the deepest point of the intercostal space.

From what has been said about the difference in levels between the exit of the root and the corresponding segment, it is clear that one and the same upper boundary of anesthesia may signify lesions at different planes, depending upon whether the spinal cord or a root is involved.

This point is of some importance in operative cases, as it adds an element of uncertainty in determining the appropriate point for an attempted incision. Of course, additional surgical evidence, such as a fracture of a vertebra, dislocation, or spondylitis, frequently indicates the proper place for the incision. When in doubt, it is advisable to begin the incision midway between the vertebra and its corresponding segment, and from there to enlarge the field of operation according to the findings.

There is still another difficulty in local diagnosis that is worth mentioning. This consists in the fact that in incomplete lesions the level of the disturbance of cutaneous sensibility depends on the situation of lesion in the cross-section of the cord, because the sensory fibers in the white matter of the spinal cord (the long tracts) corresponding to individual segments are not mixed together, but occupy different parts

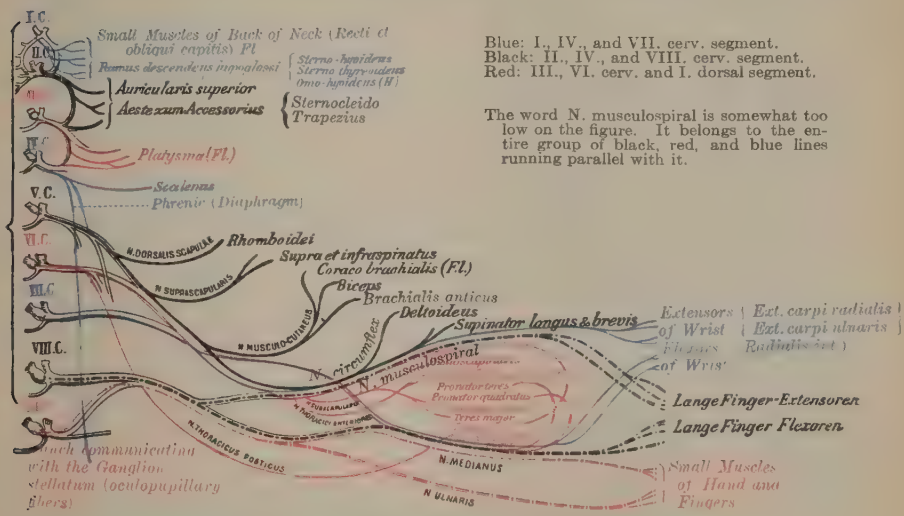


Fig. 462.—Spinal motor nerves from cervical plexus (Kocher).

of the cross-section. The laws governing the position of these long tracts are as yet not accurately determined. One thing only is certain, viz., that the posterior divisions of the sensory tracts seem to be displaced farther from the median line the lower their point of origin. In consequence of these relations the boundary of sensibility in lesions involving the cross-section of the cord unequally may (according to the topography of the lesion) correspond to the affected segment or may even lie considerably lower than in complete destruction of the segment. This applies not only to lesions which involve the cross-section irregularly, because they develop in the interior of the cord (myelitis, hemorrhage), but occasionally also to those causing pressure (trauma, spondylitis) because here also the different parts of the cross-section may suffer in varying degree. Very frequently, in injuries affecting the cord from without, the more central portions, because of their lesser consistence, are more seriously affected than the peripheral, for the same reason that

myelitic softening and hemorrhages are most commonly located in the center of the cord, so that it scarcely needs to be emphasized that the rules for localization are to be applied strictly only when we are convinced that the transverse lesion affects the entire cross-section equally. This is practically very difficult. Among other aids, the condition of the reflexes may be utilized to decide the question. The more complete the involvement of the spinal cord cross-section, the more decidedly the reflexes are affected. (See p. 996 et seq.)

Segmental Localization of Motility.—Kocher has represented the motor segmental localization in the two plates Figs. 462 and 463. They are based upon his own observations and upon the well-known atlas of Flower[1] and the works of Risien Russel[2] and Thoburn.[3] The

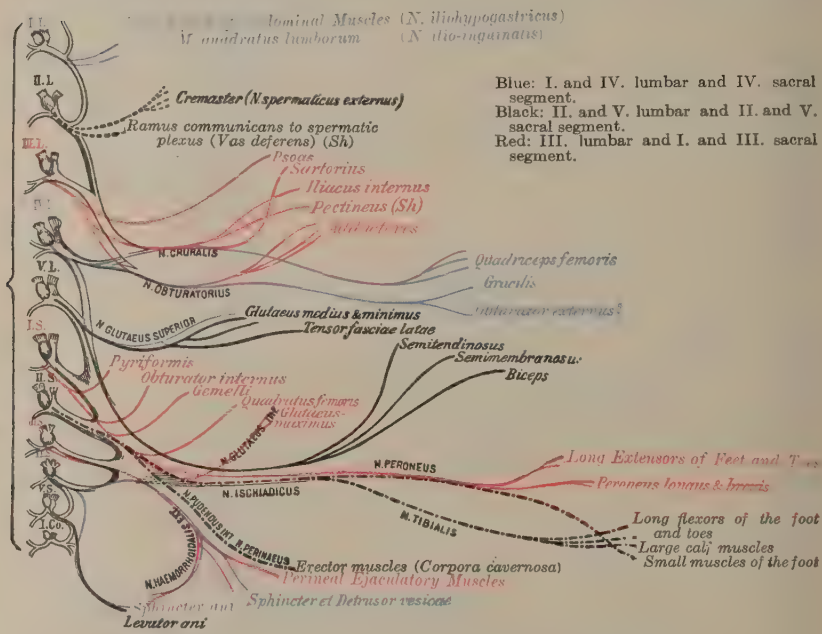


Fig. 463.—Spinal motor nerves from lumbar and sacral plexus (Kocher).

names of the great nerve-trunks composed of the fibers from the different roots are printed in black capital letters, while the names of the individual branches are printed in italics and agree in color with the corresponding segments, *i. e.*, the corresponding motor roots.

According to Kocher, these plates illustrate the following facts about the segmental motor innervation of the dorsal cord: First to twelfth dorsal segments supply the spinal muscles; first to eleventh

[1] Atlas schématique de système nerveux; translated by Duprat and Dejerine.

[2] Experimental Investigation of the Nerve Roots of the Lumbosacral Plexus, etc., Proc. of the Royal Society, vol. liv; and Experimental Investigations of the Nerve Roots of the Brachial Plexus of the Dog, Pathologic Laboratory of University College, 1892.

[3] Loc. cit.

dorsal segments supply the intercostal muscles; seventh to twelfth dorsal segments supply the abdominal muscles; first to fourth dorsal segments furnish the sympathetic nerves to the head, neck, heart, and lungs; fifth to ninth dorsal segments furnish the sympathetic nerves to the intestinal canal and to the abdominal glands (superior splanchnic nerve); tenth to twelfth dorsal segments furnish sympathetic nerves to the testicles, bladder, and rectum (inferior splanchnic nerve, internal spermatic plexus, and inferior mesenteric plexus).

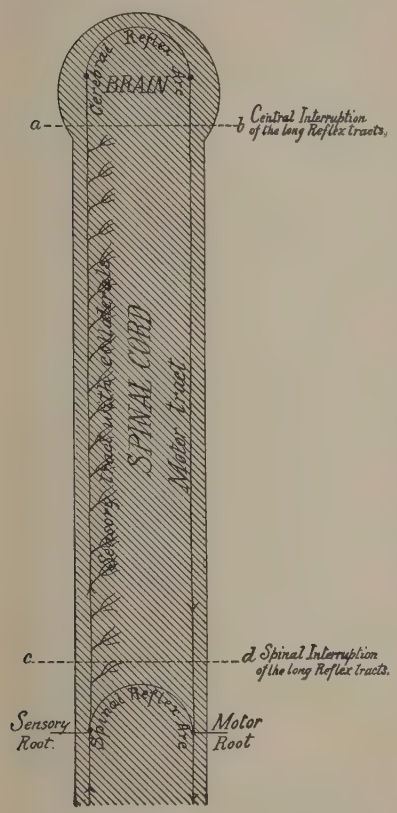


Fig. 464.—Diagram of a cerebronuclear (cutaneous) reflex to illustrate the connection between short (segmental) and long reflex tracts.

In this diagram only the cerebral reflex arc is represented completely. But the numerous collaterals (supplied with terminal twigs) show that, in addition to the shortest (segmental) circuit and to the cerebral arc, numerous spinal lateral circuits must be taken into account. This shows how incorrect it is to speak of reflex centers.

This figure explains at the same time the doctrine of reflex stasis in transverse lesions of the cord which was discussed upon p. 994. It explains why, beneath the lesion, a reflex stasis, *i. e.*, increase, and, later, abnormality of the reflexes, and, finally, pathologic reflexes, would result from a transverse lesion (*c d*); whereas, if the lesion be at *a b* in the brain, there will be no reason for any reflex stasis, because of the countless paths of escape for the sensory irritation. Therefore, a destruction of the cerebral arc is much more apt to enfeeble the reflexes. For the sake of simplicity we have omitted any representation of the bilateral course of the tracts.

Segmental Localization of the Reflexes.—By the diagrams of the motor and sensory segmental innervation of the spinal cord (Figs. 462, 463, and 357–359), the reflexes may be localized at the appropriate segments. Their value for the local diagnosis of the level of a cross-lesion is evident. The shortest reflex tracts in the spinal cord must be contained in that portion situated between the entrance of the sensory and the motor roots which conduct the reflex in question. If one know the segment which receives the sensory irritation exciting the reflex and the segment which sends out the motor fibers inner-

vating the reflex movement, then between the two must be situated the shortest intraspinal reflex tract. This was formerly spoken of as the "reflex center." There is, of course, no question of any actual reflex center, for we have learned that there is no actual transformation of the sensory reflex impulses in one group of ganglion-cells directly to the motor limb of the so-called reflex arc. At most, such an idea can assist our conception only as a diagram does. In reality, the reflex tracts comprise numerous ganglion-cells intercalated one after the other, as well as manifold lateral connections. (See p. 990 et seq. for the modern idea of the origin of the reflexes.) The shortest path of a reflex lies between the entrance of the sensory and the exit of the motor root of the reflex arc; but this does not mean that in normal cases the reflex always proceeds only by this shortest path. On the contrary, we have already seen upon p. 993 et seq. that an upper reflex arc reaching to the brain must ordinarily be innervated at the same time, and that the shortest path can be exclusively affected only in interruptions of spinal cord conduction below the lesion, as a result of reflex stasis. Fig. 464 may recall this conception to the reader. It has been more minutely explained upon p. 993. Without any further explanation it is evident from clinical experience with hemiplegia (p. 992) that only for the tendon reflexes does the interference in the reflex arc normally occur exclusively by the shortest way (between the entrance of the sensory and the exit of the motor roots). Clinically, these shortest reflex paths are important, for, as shown in Fig. 464, in a complete cross-lesion of their segment of the spinal cord the reflexes in question must be lost, because naturally all longitudinal accompanying circuits are interrupted as well. On the contrary, we must emphasize the fact that if the shortest path is anatomically intact, the reflex in question may be either preserved or lost, depending upon whether the reflex normally proceeds by the shortest path or by a longer path, whether the latter is free or interrupted, and whether the reflexes are diminished by the indirect action of a lesion lying farther above, which causes inhibition or circulatory disturbances, or (p. 990), conversely, reflex stasis. In other words, preservation of a certain reflex shows that the segment of the spinal cord uniting its motor and sensory nerve-roots must still possess, at least, partial conductivity; whereas the loss of such a reflex suggests an interruption of the corresponding segment of the spinal cord, although it does not in any way prove such interruption with certainty.

Older Views

In concluding this presentation of the segmental localization of the spinal cord, derived from the most recent sources, it seems necessary to include in the following pages the most essential of the older views upon this topic. The frequent contradictions which exist between individual views prove how unsettled this question still remains, and show that accurate clinical and pathologico-anatomic examinations will not only supply numerous corrections, but will extend our knowledge as well. These findings, especially where they concern the reflexes and their relation to the segments, must be critically examined for light upon the genesis of the reflexes. (See pp. 990 and 993.) Thus far the comparison of the conformity and non-conformity of individual views has been the only method of judging the accuracy of the data. In the discussion certain experiments performed upon animals are not excluded, because they are useful for the purpose of criticism. In this connection the observations made by Ferrier and Yeo upon apes by irritating the motor nerve-roots are especially valuable, particularly because many other experiments, especially the well-known researches of Horsley and Beevor upon the cerebral cortex (see Figs. 425 and 426), show the most intimate analogy between the nervous

system of apes and that of man. Even the gross anatomy of the plexuses of the extremities must be taken into account, and, therefore, finds a place in the following:

CLINICAL DATA

Localization of the Functions in the Different Spinal-cord Segments.—(From Starr-Edinger-Bruns.[1]*)*

Segments.	Motor roots for—	"Reflex centers"[2] for—	Sensory roots (cutaneous innervation) for—
First cervical nerve.	Small muscles of the neck, Sternocleidomastoid and trapezius.		
Second to third cervical nerves.	Sternocleidomastoid, Trapezius, Scaleni and neck muscles (complexus, splenius, longus colli).	.....	Neck and occiput.
Fourth cervical nerve.	Complexus, Splenius, longus colli, Levator scapulæ, Diaphragm (phrenic nerve), Supra- and infraspinati, Deltoid, Biceps and coracobrachialis, Supinator longus, Rhomboidei.	Dilatation of the pupils from a sensory stimulation of the neck (fourth to seventh cervical nerve).	Neck, Upper shoulder region, Outside of the arm to the second rib.
Fifth cervical nerve.	Diaphragm (phrenic nerve), Deltoid, Biceps, brachialis anticus, Coracobrachialis, Supinator longus and brevis, Pectoralis major (pars clavicularis), Serratus magnus, Rhomboidei, Teres minor, Latissimus dorsi.	Scapular reflex (fifth cervical nerve to first dorsal nerve). Tendon reflexes of the muscles and tendons about the elbow-joint (fifth to sixth cervical nerve).	Posterior aspect of the shoulder and arm. Outside of the arm and forearm.
Sixth cervical nerve.	Biceps, Brachialis anticus, Pectoralis major (pars clavicularis), Serratus anticus major, Triceps, Extensors of the hand and fingers, Pronators.	Extensor reflexes of the arm and forearm.	Outside of the forearm.
Seventh cervical nerve.	Long head of the triceps, Extensors of the hand and finger, Flexors and pronators of the hand, Pectoralis major (pars costalis), Subscapularis, Latissimus dorsi, Teres major.	Flexor reflexes.	Radial area of the hand and part of the median area.

[1] Starr collected the older data from the clinical examinations of localized spinal-cord lesions, which are recorded as late as 1888.

[2] This expression (see p. 1152 et seq. and Fig. 464) is incorrect, and signifies here merely the shortest reflex arc, and, therefore, that segment of the cord which includes the sensory and motor roots of the reflex in question.

Localization of the Functions, etc.—(Continued.)

Segments.	Motor roots for—	"Reflex centers" for—	Sensory roots (cutaneous innervation) for—
Eighth cervical nerve.	Flexors of the hand and fingers, Small muscles of the hand.	Dilator of the pupil and smooth muscles of the orbit, with first dorsal nerve.	Median area. Ulnar area.
First dorsal nerve.	Extensors of the thumb, Small muscles of hand, Muscles of ball of thumb and little finger.	Dilator of the pupil and smooth muscles of the orbit in conjunction with eighth cervical nerve.	Ulnar area.
Second to twelfth dorsal nerve.	Back muscles, Abdominal muscles.	Abdominal reflexes in the fourth to eleventh dorsal segments; according to Dinkler, in the ninth to twelfth dorsal segments.[1]	Skin of the breast, back, abdomen, and upper gluteal region.
First lumbar nerve.	Abdominal muscles, Psoas, Sartorius.	Cremaster reflex.	Skin of the pubic region, anterior surface of the scrotum.
Second lumbar nerve.	Psoas, Sartorius, Flexors of the knee (Remak?), Quadriceps femoris.	Cremaster reflex. Patellar tendon reflex (second to fourth lumbar nerve).	Outside of the hip region.
Third lumbar nerve.	Quadriceps femoris, Psoas and pectineus,[1] Inward rotators of the thigh, Abductors of the thigh.	Patellar tendon reflex (second to fourth lumbar nerve).	Anterior and inner side of the hip region.
Fourth lumbar nerve.	Adductors and abductors of the thigh, Tibialis anticus, Peroneus longus, Flexors of the knees (Ferrier?).	Patellar tendon reflex (second to fourth lumbar nerve). Gluteal reflex (fourth to fifth lumbar nerve).	Inner side of the hip and leg as far as the ankle. Inner side of the foot.
Fifth lumbar nerve.	External rotators of the hip, Flexors of the knees (Ferrier?), Flexors of the foot, Extensors of the toes, Peronei.	Gluteal reflex (fourth to fifth lumbar nerve).	Posterior side of the hip, of the thigh, and external part of the foot.
First to second sacral nerves.	Flexors of toes and foot, Small muscles of feet, Peronei.	Plantar reflex. Bladder and rectal center (Sarbo).	Posterior side of the thigh, outside of the leg and foot.
Third to fifth sacral nerves.	Perineal muscles.	Achilles tendon reflex. Bladder and rectal center.	Posterior side of the scrotum, Perineum, anus, sacral region.

[1] In regard to local diagnosis these data must be accepted with reserve, because it is manifest that they refer merely to the entrance and exit of centripetal and centrifugal segments of the lowest reflex arc, and because, as the abolition of the abdominal reflex on the paralyzed side in cerebral hemiplegia indicates, the abdominal reflex arc normally includes the brain.

W. Thoburn[1] has independently obtained results that are similar to but not in complete accord with those of Kocher.

BRACHIAL PLEXUS (Motor Innervation)

Cervical nerves:	
Fourth	Supra- and infraspinatus, teres minor (?).
Fifth.	Biceps, brachialis anticus, deltoid, supinator longus, supinator brevis.
Sixth.	Subscapularis, pronators, teres major, latissimus dorsi, pectoralis major, triceps, serratus major.
Seventh.	Extensors of the wrist.
Eighth.	Flexors of the wrist.
Dorsal nerves:	
First.	Small muscles of the hand.

LUMBOSACRAL PLEXUS

Lumbar nerves:	Motor Distribution.	Sensory Distribution.
First.	(?)	The iliohypogastric and ilio-inguinal nerves.
Second.	(?)	External (?) and upper region of the thigh.
Third.	Sartorius, Adductors, Flexors of the thigh.	Anterior surface of the thigh, below the region supplied by the second lumbar nerve.
Fourth.	Extensors of the knee, Abductors of the thigh.	Anterior and inner surface of the thigh.
Fifth.	Flexors of the leg.	Posterior side of the thigh, except the territory supplied by the sacral roots.
Sacral nerves:		
First.	Calf muscles, Gluteal muscles,	Narrow strip on the posterior surface of the thigh and leg, sole of foot.
Second.	Peroneal muscles, Dorsal flexors of the ankle-joint, Small muscles of the foot.	A part of the dorsum of the foot.
Third.	Nervi erigentes, Perineal muscles.	Perineum, external genitals.
Fourth.	Bladder and rectum.	Posterior surface of the thigh.

Dinkler's[2] observations, made in Erb's clinic, upon the localization of the abdominal reflexes, should be mentioned. He found that the abdominal reflexes have their shortest circuit in the lowest part of the dorsal cord, that the middle and lower abdominal reflexes (p. 988) belong to the tenth, eleventh, and twelfth intercostal nerves and their corresponding spinal segments, while the upper abdominal reflex is limited to the tract of the ninth and possibly, also, of the eighth dorsal nerves. This tallies with the segmental localization of the corresponding cutaneous areas. (See Fig. 457, p. 1145.) Still, these statements apply only to the shortest circuit of the reflex arc and do not exclude the longer reflex arcs reaching further up through the affected sections which have been shown at autopsy and in cerebral hemiplegia. (See foot-note, p. 1154.)

For the local diagnosis of lesions of the cervical cord the reader should consult Kraus's article (from Kahler's Clinic), Zeit. f. klin. Med., 1891, vol. xviii, p. 343. In conformity with Fräulein Klumpke's experiments on animals, he found that in man the sympathetic oculopupillary fibers, whose paralysis causes myosis and retraction of the globe with sympathetic ptosis (Paralysis of Müller's Smooth Orbital Muscle, see p. 1046), leave the spinal cord with the motor root of the first dorsal nerve. These are the fibers which connect the principal trunk of the sympathetic with the so-called ciliospinal center of the spinal cord. The latter was localized by Budge between the sixth cervical and the second dorsal segments. Kraus's statements coincide with

[1] A Contribution to the Surgery of the Spinal Cord, London, 1889.
[2] Zeit. f. Nervenheilk., 1892, vol. ii, p. 325.

Gowers gives the following table:[1]

Motor functions.	Nerves.	Motor functions.	Nerves.	Sensory functions.	Reflex.
	C 1	Small rotators of head,[2]	1		1
Sternomastoid, upper neck muscles, upper part of trapezius.	2	Depressors of hyoid.	2	Scalp,	2
	3	Levator anguli scapulæ.	3	Neck and upper part of chest.	3
	4, 5	Diaphragm.	4, 5	Shoulder.	4, 5
Lower neck muscles, middle part of trapezius.	6	Serratus, Flexors of elbow, Supinators. (Shoulder muscles.)	6	Arm, outer side. Radial side of forearm and hand, thumb.	6
	7	Extensors of wrist and fingers.	7	Arm, inner side, ulnar side of forearm and hand, tips of fingers.	7 (Scapular.)
	8	Extensors of elbow, Flexors of wrist and fingers, Pronators.	8	Front of thorax.	8, 1 (Scapular.)
	D 1	Muscles of hand.	1	Ensiform area.	2, 3, 4
Lower part of trapezius and dorsal muscles.	2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12	Intercostal muscles.	2, 3, 4, 5, 6, 7	Abdomen (Umbilicus 10).	5, 6, 7 (Epigastric.)
			8, 9, 10, 11, 12	Buttock, upper part.	8, 9, 10, 11, 12 (Abdominal.)
		Abdominal muscles.	1, 2	Hip and scrotum.	1, 2 (Cremaster.)
	L 1		3	Thigh: Outer side.	3 (Knee-jerk.)
			4	Thigh: Front.	4 (Gluteal. Footclonus.)
Lumbar muscles.	2, 3	Cremaster, Flexors of hip.	5	Thigh: Inner side. Leg, inner side.	5 (Gluteal. Footclonus.)
	4	Extensors of knee, Adductors of hip,	1	Buttock, lower part.	
Peroneus I. Flexors of ankle, extensors of ankle.	5	Extensors and abductors of hip.	2	Back of thigh.	
		Flexors of knee.	3	Leg and foot: except inner part.	1, 2 (Plantar.)
	S 1	Small muscles of foot.	4	Perineum and anus.	3
	2		5	Skin of coccyx and anus.	4
	3, 4, 5	Perineal and anal muscles.			5
	Co.		*Co.*		*Co.*

[1] Handbook of Nervous Diseases, vol. i, p. 252.

[2] Especially the obliquus capitis inferior, which turns the head to the same side. —Author.

L. Jakobsohn's[1] anatomicopathologic findings in man. This writer found the lateral horn corresponding to the first dorsal segment diseased in a lesion of the oculo-pupillary sympathetic fibers.

EXPERIMENTAL DATA

Ferrier and Yeo,[2] in irritation experiments upon apes, obtained the following results in reference to the assignment of individual muscles to the motor-nerve roots:

Motor Roots of the Brachial Plexus (after Ferrier and Yeo).

Fourth Cervical Nerve.—Deltoid, rhomboids, supra- and infraspinatus, teres minor, brachialis anticus, supinator longus, extensors of the hand and fingers, diaphragm.

Fifth Cervical Nerve.—Deltoid (clavicular portion), biceps, brachialis anticus, serratus anticus major, supinator longus, extensors of the hands and fingers.

Sixth Cervical Nerve.—Latissimus dorsi, pectoralis major, serratus magnus, pronators, flexors of the wrist (?), triceps.

Seventh Cervical Nerve.—Teres major, latissimus dorsi, subscapularis, pectoralis major, flexors of the hand and fingers (median), triceps.

Eighth Cervical Nerve.—Long flexors, flexor carpi ulnaris, small muscles of hand, extensors of the hand and fingers, long head of the triceps, pectoralis major (?).

First Dorsal Nerve.—Small muscles of the hand.

Motor Roots of the Lumbosacral Plexus (after Ferrier and Yeo).

Third Lumbar Nerve.—Psoas, sartorius, adductors, extensor cruris.

Fourth Lumbar Nerve.—Extensors of the thigh, extensor cruris, peroneus longus, adductors.

Fifth Lumbar Nerve.—Flexors and extensors of the toes, tibial muscles, calf muscles, peroneal muscles, external rotators of the thigh, flexors of the leg (biceps, semitendinosus, etc.).

First Sacral Nerve.—Calf muscles, flexors of the leg, flexor hallucis longus, small muscles of the foot.

Second Sacral Nerve.—Small muscles of the foot.

Dastre and Morat found, in experimenting upon animals, that most of the vasomotor and sweat-secretory fibers for the face first leave the cord with the second to sixth dorsal nerves.

Additional experimental results worth mentioning are those obtained by Nawrocki and Skabitschewsky upon the origin of the motor and sensory fibers for the bladder of the cat. They found that the motor nerves of the bladder leave the spinal cord by two paths—an upper and a lower. The upper leads to the vesical plexus from the fourth and fifth anterior lumbar roots; the lower from the second and third anterior sacral roots. The sensory fibers are partly sympathetic, partly cerebrospinal, in origin; the former are contained exclusively in the hypogastric nerve, the latter in the four upper posterior sacral roots. (See also L. B. Müller's data on p. 1167 et seq.)

Rossolimo found in dogs that the center for the *anal reflex* (p. 988) was situated in the region of the third and fourth sacral nerves.

PURELY ANATOMIC DATA

Herringham[3] obtained the following results in regard to motor innervation from purely anatomic researches upon the course of the individual motor nerve-roots through the brachial plexus:

Fifth Cervical Root.—Biceps, brachialis anticus, subscapularis, deltoid.

Sixth Cervical Root.—Pectoralis major, biceps, brachialis anticus, pronator teres, flexor carpi radialis, thenar muscles, subscapularis, teres major, deltoid, supinator longus and brevis, extensor carpi radialis, longior and brevior.

Seventh Cervical Root.—Pectoralis major and minor, coracobrachialis, flexor sublimis, latissimus dorsi, triceps, radialis externus, longus and brevis.

[1] Zeit. f. klin. Med., 1899, vol. xxxvii.
[2] Brain, 1882, vol. iv, p. 226.
[3] Proc. Royal Soc., 1886, No. 243, p. 225.

Eighth Cervical Root.—Pectoralis major and minor, flexor sublimis, latissimus dorsi, triceps.

First Dorsal Root.—Pectoralis major and minor.

At all events, we have anatomic examinations to thank for the knowledge that the *phrenic nerve*, to a large extent, derives its fibers from the *fourth motor*

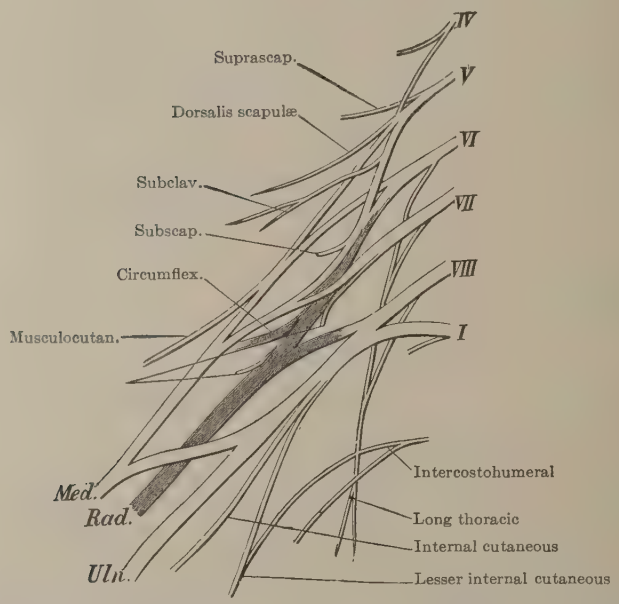


Fig. 465.—Plexus brachialis: *IV, V, VI, VII, VIII, I*, Anterior branches of the five lowest cervical nerves and of the first dorsal nerve. Of the branches extending anteriorly, only the subclavius nerve is represented (after Gegenbaur).

cervical root, and sometimes a part from the third and fifth; the *occipitalis magnus* derives its fibers from the second, the *occipitalis minor* from the first, second, and third, and the *auricularis magnus* from the third and fourth *sensory* cervical roots.

The annexed figures (465 and 466) and Gegenbaur's *Lehrbuch der Anatomie* may be consulted for a general idea of the origin of the plexuses for the extremities, and their subdivisions into the peripheral nerves.

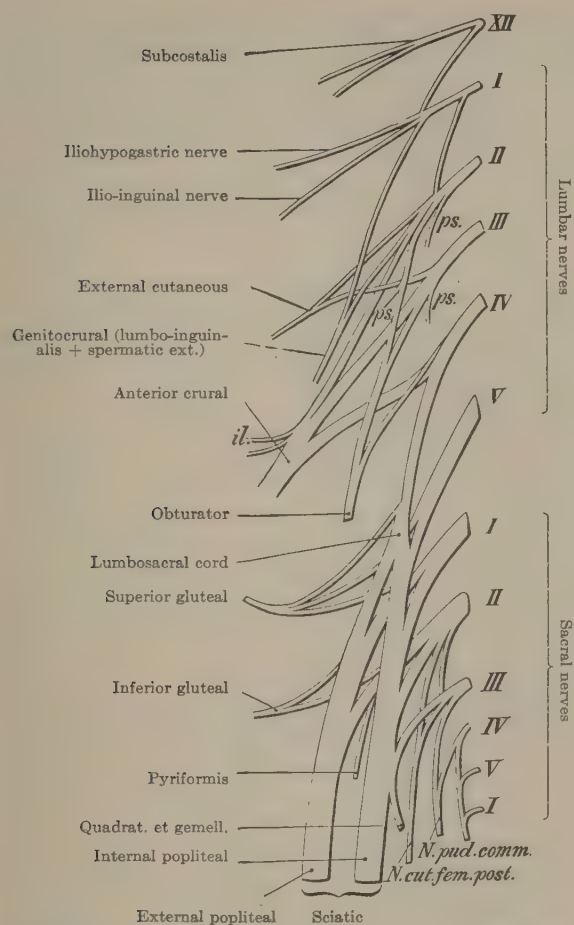


Fig. 466.—Lumbosacral plexus: *ps*, Branches to the psoas muscle; *il*, branches to the iliac muscle (after Gegenbaur). In the sacral division, the sciatic plexus which forms the sciatic nerve is split up into its component parts (according to Paterson).

(*c*) Topography of the Lumbosacral Cord, of the Conus Terminalis, and of the Cauda Equina

In order to make a differential diagnosis and determine the definite localization of affections of the cauda equina, of the lumbar and sacral cord, and of the conus terminalis, it is very essential to possess an exact knowledge of the topographic relations of this region and especially of the situation of the points of origin of the lumbar and sacral nerves from the cord, as compared with the vertebræ or the points of exit of the nerve-roots from the spinal-cord canal. The following plates will serve for orientation.

The limits of the conus terminalis have not yet been very sharply defined. Raymond puts its upper borders sufficiently high to include the centers or the medullary origins of the last three sacral nerves. Such delimitation conforms both with the requirements of descriptive anatomy, *i. e.*, with the boundaries of

the actual wedge-shaped terminal portion of the spinal cord, and with those of clinical experience, *i. e.*, the clinical picture of a lesion of the second lumbar vertebra.[1] In lesions of the conus terminalis, both motility and sensibility of the lower extremities are practically intact, but the functions of the bladder and rectum are disturbed, and there is an anesthesia of the perineum, the inferior gluteal region, and of a zone upon the back of the thigh, which is supplied by the posterior femoral cutaneous nerve. This does not entirely coincide with the topography of sensibility disturbance pictured upon p. 1144. A lesion of the lower part of the cauda equina will, of course, produce a similar clinical picture.

Fig. 468 shows, according to Schultze, that the clinical picture of still higher lesions of the lowest portion of the cord may be simulated by lesions of the cauda

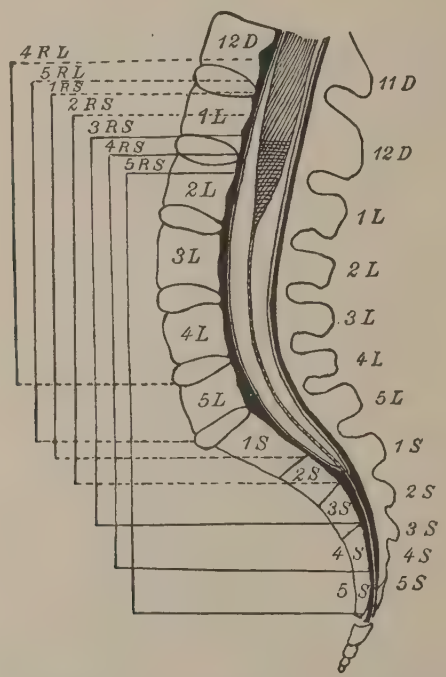


Fig. 467.—The lower end of the vertebral column and its topographic relation to the lumbar and sacral cord, and to the origins and exits of the lumbar and sacral nerves. The cross-shaded portion represents the conus terminalis, according to Raymond's definition (see the text), to which is attached the filum terminale. Between it and the wall of the vertebral canal (the part in white) the cauda equina passes. The upper horizontal lines indicate the heights at which the nerve-roots spring from the spinal cord; and the lower horizontal lines connected with the upper ones by means of vertical lines indicate the exits of the corresponding roots from the vertebral column. The vertical lines thus represent the lengths of the separate roots of the cauda equina (after Raymond[2]).

equina. It is quite plain from the drawing that the lesion A, at the most inferior portion of the spinal cord, and the lesion B, at the height of the third lumbar vertebra, which injures the cauda equina, will produce the same motor and sensory disturbances of the sciatic region and will not involve the crural and obturator region (second to fourth). A hyperesthesia of the crural region, or a very slight

[1] A Schiff (from Schrötter's Clinic), A Case of Hematomyelia of the Conus Terminalis, Zeit. f. klin. Med., 1896, vol. xxx, p. 87.

[2] Raymond, Sur les affections de la queue de cheval, Nouvelle inconographie de la Salpêtrière, 1895, Nos. 1 and 2.

initiatory involvement of it, may occur in either case, because the lesion A (represented by shading) affects the spinal cord itself above the origin of the crural fibers, whereas the lesion B involves the same fibers laterally and lower down at the height of the third lumbar vertebra.

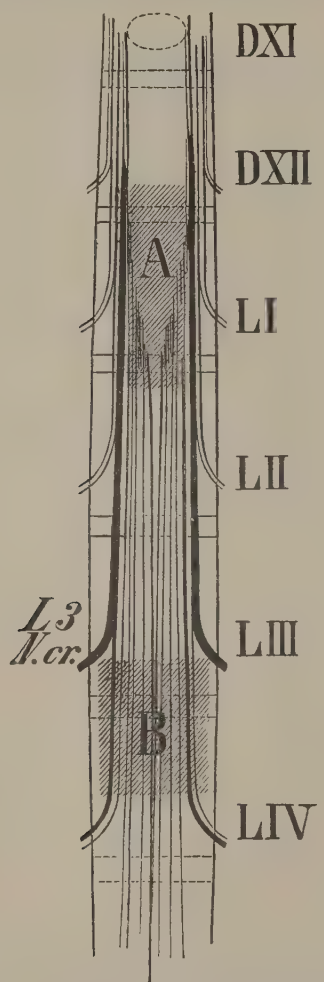


Fig. 468.—Topography of the cauda equina, showing its relation to the vertebral column and to the lower end of the spinal cord (⅔ natural size). Schultze gives the following explanation: "The lower end of the lumbar enlargement is found at the level of the first lumbar vertebra; the third lumbar nerve (heavy black line), with its crural and obturator fibers, arises at different levels (the right side is here indicated lower than the left); as indicated, in the upper part of the lumbar enlargement, according to Gerlach, between the spinal processes of the eleventh and twelfth[1] dorsal vertebræ, a height which, according to the original investigations of Schiefferdecker, corresponds to the lower part of the body of the twelfth dorsal vertebra" (after Schultze and Schiefferdecker[2]). The position of the conus terminalis is higher here than in Fig. 467.

[1] On account of the oblique downward direction of the spinous process.

[2] Schultze, Zur Differentialdiagnose der Verletzungen der Cauda equina und der Lendenanschwellung, Deut. Zeit. f. Nervenheilk., 1894, vol. v, p. 247.

4. THE VESICAL AND RECTAL FUNCTIONS

The Mechanism of the Vesical and Rectal Functions under Physiologic and Pathologic Conditions

It is difficult to understand the vesical and rectal disturbances occurring in diseases of the nervous system, since our knowledge of the physiologic evacuation of the bladder and rectum is still quite incomplete and contains much that is hypothetic. In studying this subject we are confronted by a special difficulty, because the old teaching that the central mechanism for the vesical and rectal functions is situated in the spinal cord has been overthrown. The prevailing opinion at present, based upon the work of Goltz, Freusberg, Ewald,[1] and particularly upon the recent work of L. R. Müller,[2] inclines to the view that the central mechanism for the vesical and rectal functions is situated in the sympathetic system. Since this question has not been absolutely decided, but requires further investigation (which may show that both conceptions possibly contain a portion of the truth), the author feels bound to give, first, the old, and then the newer, teaching, and to conclude with a few remarks as to the possibility of combining the two theories. (See p. 1169.)

I. The Old Conception of the Vesical and Rectal Functions, in which the Central Mechanism was Supposed to be in the Spinal Cord.—*The Physiologic Mechanism of the Vesical Functions.*—The following diagram of the innervation of the bladder (Fig. 469) should be of assistance in comprehending the clinical features of the question.

Bl represents the bladder. The detrusor muscle is represented by a thick line, the mucous membrane by a dotted line. The voluntary sphincter, which is composed of the different voluntary muscles surrounding the urethra[3] (Krause's musculus urethralis) is represented by two circular cross-sections at both sides of the bladder orifice, *b′*.

The points *a*, *b*, *c*, represent the so-called bladder centers, as they have been thus far usually conceived.

a corresponds to a sensory cell, or, better expressed, a cell in connection with the sensory terminal arborizations of the tract *a* to *a′*; *b* represents a motor cell for the sphincter; *c* represents a motor cell for the detrusor. *a* should be conceived to be connected with the mucous membrane by means of the sensory tract *a* to *a′*; *b* with the sphincter by the motor tract *b* to *b′*; and *c* with the detrusor by the motor tract *c* to *c′*.

The normal bladder reflex takes place in this way: When the bladder fills, the mucous membrane stimulates the tract *a′* to *a*. From *a* the stimulation proceeds to the sphincter center *b*, and from there, in the form of a tonic innervation, to the sphincter, *b′*, which then shuts the bladder more powerfully. When the filling increases still further, until a certain degree of distention is reached, a more intense stimulation *a′* to *a* proceeds from *a* even to *c*, and finally causes a contraction of the detrusor. The bladder will then be emptied. The normal bladder reflex, therefore, consists of two acts: the closing reflex and the emptying reflex. We have included in our diagram the longitudinal

[1] Pflüger's Arch., vols. viii, ix, lxiii.
[2] Zeit. f. Nervenheilk., vol. xxi, parts 1 and 2.
[3] The so-called "smooth sphincter" probably plays no important physiologic function.

tracts, which have an influence upon emptying the bladder; they have been demonstrated both physiologically and clinically, ascending and descending within the spinal cord. They are:

1. The tract *a* to *A*, a sensory tract leading to the brain, which informs us how full the bladder is.

2. The tract *B b b′*, subserving the voluntary innervation of the sphincter. As we cannot voluntarily innervate the detrusor, it probably does not possess an analogous tract.

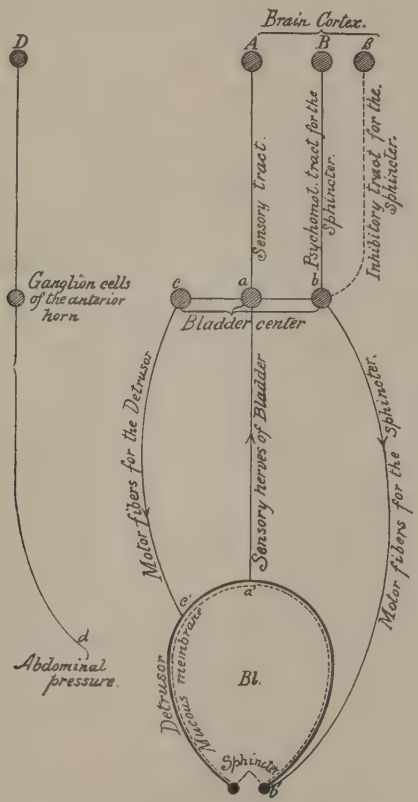


Fig. 469.—Scheme for the physiologic mechanism of the bladder functions.

3. The tract *β* to *b*, which inhibits the tonus of the sphincter. Since there is no voluntary detrusor tract, *β b* presides over the voluntary emptying of the bladder.

4. The tract *D* to *d*, inserted upon the left of the annexed diagram, comes from the brain and innervates the abdominal muscles concerned in straining movements, therefore, assisting in forced voluntary emptying.

Voluntary emptying of the bladder takes place normally by means of these longitudinal tracts. For, after we have become cognizant of

the bladder distention and of the necessity for emptying it by means of the tract a' to a, we voluntarily relax the sphincter by an innervation along $B\ b\ b'$. This gives free scope to the reflex innervation of the detrusor by the path $a'\ a\ c\ c'$. Under some circumstances, when urination is urgent, abdominal pressure is called in to assist by way of the tract $D\ d$.

It should, of course, be understood that the longitudinal tracts, both sensory and motor, are bilateral,[1] and that their radiations on each side are in connection with both hemispheres of the brain. One hemisphere would, therefore, be sufficient to care for the voluntary function (both sensory and motor) of the bladder (as in the case of the eye muscles, p. 1041, Fig. 403).

A Brief Consideration of the Behavior of the Bladder Function in Various Lesions of the Nervous System

Functions of the Bladder in Cerebral Affections.—Since ordinarily only one hemisphere is involved in diseases of the brain and, therefore, not all the fibers passing from the brain to the spinal cord are injured, and since the long tracts to the bladder are bilateral, lesions of the long tracts usually do not produce disturbances of the bladder in cerebral diseases, except from affections of the medulla and the pons. In the latter case, on account of the close proximity of the bilateral tracts, results are like those produced by lesions of the spinal cord. (See below.)

Bilateral cerebral lesions, on the contrary, may lead to disturbances in the bladder function, especially if they are diffused. This is because the bladder tracts are not arranged in the brain compactly in a bundle, but seem to spread out diffusely. These disturbances are ordinarily associated with disturbances of consciousness. An unconscious person allows his urine to escape because he has no will-power and no sensation. He is obliged to trust everything to the reflexes. The bladder reflex may be entirely unaffected, so that from time to time the bladder is emptied quite normally, even though unconsciously and involuntarily. Quite severe conditions of unconsciousness may lead to retention of the urine, with an eventual overflow of the overfilled bladder (paradoxic incontinence). These cases are most readily explained, as in spinal-cord affections (see below), by assuming loss of inhibition of the sphincter reflexes. The bladder may be similarly affected by brain injury in any serious illness, such as typhoid fever, etc.

Functions of the Bladder in Diseases of the Spinal Cord.—The following possibilities are conceivable:

1. The bladder center itself is injured. Both the sphincter and the detrusor reflexes are lost. The bladder behaves like a mere bag. The urine trickles continually, of course, only after the bladder has been more or less distended, as a certain pressure of the urine is required to open the urethra. This is a condition of incontinence, with a more or less marked retention (incontinence of the distended bladder, incontinentia paradoxa). Sounding by means of a catheter proves the existence of an actual bladder paralysis. The opposition of the sphincter is lost, and the contents of the bladder can be quite easily expressed by manual pressure upon the lower abdominal region.

[1] For the sake of simplicity our diagram shows only a unilateral arrangement of the tracts.

2. The bladder center is intact, the lesion is located above the center, and only the long tracts which lead to the brain are injured. The influence of volition upon emptying the bladder will be more or less completely lost. If the injury to the long tracts be complete (and this is the usual effect of any pronounced focal lesion of the spinal cord, everything being so crowded together in a narrow cross-section), the patient will not be conscious of any distention of the bladder, nor possess any voluntary influence over it. One would naturally suppose that at least the reflex activity of the bladder would be normal; but this is only rarely true. To be sure, in exceptional cases of a cross-lesion of the spinal cord above the so-called bladder center, patients (especially children) will empty the full bladder, from time to time, in a perfectly normal fashion (pure enuresis), but entirely involuntarily. Perhaps this type of disturbance occurs only in the less complete interruptions of conduction. But much oftener these patients suffer from urinary retention; the bladder becomes more and more distended; the sphincter finally gives way; and the urine trickles out. Such a condition of incontinence with an overfilled bladder is called *paradoxic incontinence*. The distinctive appearance of decided retention, which is always much more pronounced in these cases than in those under the first head, is to be explained by assuming that in extensive cross-lesions of the spinal cord above the bladder center, the tract inhibiting the sphincter reflex (*3 b*, Fig. 469, p. 1163) is injured as well as the other long tracts. Analogous to the increase of tendon reflexes usually accompanying these cases, the tonus of the sphincter is naturally accentuated enough to overcome the power of the detrusor, and retention consequently ensues.

3. The lesion is situated below the bladder center. Since both sensory and motor fibers for the bladder run down from the bladder center within the spinal cord for a short distance before they pass out, such a focal lesion will partially interrupt the reflex arc of the bladder. The effect must, therefore, be similar to that of a lesion of the bladder center itself. (See 1, p. 1164.) As we do not know just where the motor and sensory bladder nerves leave the spinal cord, it is conceivable that, below this spot, an area in the spinal cord might exist injury of which would not affect the bladder function because the bladder nerves would already have left the spinal cord. Clinical experience, however, points to the improbability of such a supposition, and the diagram (Fig. 463, p. 1150), representing a deep exit of the motor nerves of the bladder, should, therefore, be considered as accurate. The statements of physiologists in regard to position of the "bladder center" are so contradictory, and the physiologic methods of examining this question are so ambiguous, that we must provisionally depend upon clinical experience. The latter suggests that the human bladder innervation is represented even at the end of the spinal cord.

The Bladder Functions in Peripheral Affections of the Bladder Nerves.—The function of the bladder is rarely disturbed in these affections, possibly because the relatively short course of these nerves renders their power of conductivity especially favorable. Still it should be remembered, in regard to the differential diagnosis between poliomyelitis and polyneuritis that bladder disturbances may appear in the latter. In any given case the type of disturbance can be easily explained by consulting the diagrams.

Another Representation of the Bladder Functions.—The preceding diagram should be regarded as wholly theoretic. It depends upon the unproved assumption of a circumscribed bladder function in the spinal cord. (See p. 1151 et seq. for arguments against such a theory.) This assumption is based upon the fact that complete paralysis of the bladder (p. 1164, No. 1) has been proved, both experimentally and clinically, to occur with disturbances in the territory of the lowest part of the spinal cord. This fact may, however, be perfectly explained in another way by assuming that the importance of the lumbar and sacral cord in controlling bladder functions depends upon the compact arrangement of the sensory and motor fibers of the bladder at their exit there from the spinal cord; whereas, higher up, they perhaps spread out diffusely through a large portion of the longitudinal and cross-sections of the cord. Although, without doubt, the shortest reflex arc (*i. e.*, the shortest connection between the sensory and motor bladder nerves) is localized in the lowest portion of the spinal cord, this does not necessarily prevent the circuit of the reflex arc from reaching high up into the spinal cord (perhaps even to the brain).[1] The pathologic affections of the bladder functions can be explained as well, and perhaps more readily, by Fig. 470 than by Fig. 469, provided that we make such an assumption and consider the mechanism of the bladder functions analogous to the mechanism of the cutaneous reflexes. (See p. 993 and Fig. 464, p. 1151.) In Fig. 470 we need to assume only that the reflex arcs for the detrusor reach high up in the spinal cord, or even as high as the brain; whereas, the sphincter reflex takes place principally by shorter tracts (in the lumbar enlargement). This conception readily explains the occurrence of retention of urine (paradoxic incontinence) in all complete cross-lesions situated above the lumbar enlargement, for the detrusor reflex would then be injured more than the sphincter reflex. This conception does not need to assume a definite center to explain the fact that severer bladder disturbances result from lesions of the lumbar enlargement, for, according to this assumption, a lesion here affects the entire centripetal and centrifugal bladder innervation. Again, it explains most readily the variations of the less typical bladder affections in which the bladder fibers for the different functions must be assumed to be variously affected; for, when we represent the reflex apparatus of the bladder (as in Fig. 470) distributed through the entire spinal cord and even to a part of the brain, it becomes perfectly natural to conceive that the bladder mechanism can be injured in manifold ways, as is especially the case in system diseases like tabes.

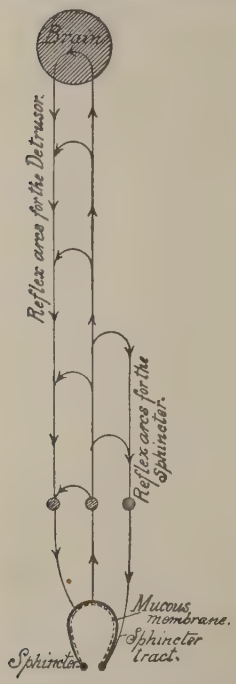


Fig. 470.—Scheme of bladder functions with superimposed reflex arcs.

So far as the voluntary control of the bladder is concerned, Fig. 470 should be regarded in the same way as Fig. 469, and should be completed by adding the voluntary tracts for the closure and relaxation of the sphincter, as well as those innervating the muscles concerned in abdominal straining.

We might add that the principle of the bladder innervation is not influenced by assuming in both Figs. 469 and 470 that parts of the reflex arc run in sympathetic tracts.

Mechanism of Emptying the Rectum under Physiologic and Pathologic Conditions.—The emptying of the rectum is accomplished in the same way as the emptying of the bladder. With the proper changes, what has been said about the latter applies to the rectum. The old conception of a rectal center localized in the lumbar enlargement of the spinal cord (see Fig. 469) becomes less probable when we assume that the

[1] The theory that the reflex tracts of the bladder reach up into the brain agrees with the fact that the bladder functions are not necessarily destroyed by focal lesions of the brain, as the tracts in question must be situated bilaterally in the brain, while most cerebral lesions only affect one side. Moreover, the exceptional cases where cerebral lesions do affect the bladder functions are most easily explained by this assumption.

reflex arcs of the rectum (like those of the bladder in Fig. 470) run far up into the spinal cord, and perhaps even into the brain. Either theory will explain (as with the bladder) the fact that lesions of the lumbar and sacral cord produce an actual paralysis of the rectum; whereas lesions higher up cause, for the most part, a decided retention of feces. Clinically, however, the picture of fecal accumulation caused by paralysis of the detrusor reflex or by increase of the sphincter tonus can be altered if the peristalsis of the upper part of the gut, which is not under the direct control of the spinal cord, be sufficient to expel the fecal masses from the rectum in spite of the retention. On the other hand, the picture of sphincter paralysis in the rectum may be modified and much less noticeable if the fecal masses be hard enough to remain in the rectum, despite a weak or absent closure of the sphincter.

II. The New Theory of Sympathetic Vesical, Rectal, and Ejaculatory Centers (*Goltz, Freusberg, Ewald, L. R. Müller*).—The theory of the spinal localization of the vesical and rectal centers has long since been shaken by the experiments of Goltz, Freusberg, and Ewald.[1] These writers demonstrated that in dogs, after the removal of the lowermost portion of the spinal cord, which presumably contained the vesical and rectal centers, the primarily disturbed vesical and rectal functions became normal after a time. The theory of the spinal localization of the centers for the vesical, rectal, and ejaculatory functions had become so deeply rooted during the preceding fifty years, however, that it continued to dominate physiologic, as well as clinical, teaching. Since L. R. Müller's recent important experiments[2] have completely confirmed those of Goltz's school and shown that the centers for the vesical and rectal functions and for the male sexual act are situated outside of the spinal cord in the sympathetic system, we must determine to what extent our clinical ideas should be revised.

The experimental results attained by Müller are essentially as follows: If the spinal cord of the dog be divided above the sacral segments, or if the sacral segments be extirpated, the result is practically the same. At first there is retention of the urine and of the feces. The bladder may be mechanically evacuated by pressure, and if this be not done regularly, the bladder overflows (paradoxic incontinence). After a time, however, this urinary and fecal retention disappears and is replaced by periodic evacuations differing from the normal only in that they are involuntary. Since this reëstablishment of periodic evacuations occurs even after complete extirpation of the lumbar and sacral cord, the central mechanism for these functions evidently must be situated outside of the spinal cord in the sympathetic system. Experiments in reference to the localization of the sexual functions in male dogs led to similar results. After the extirpation of the sacral and of a great portion of the lumbar cord, the dogs are capable not only of erection, but also of ejaculation. The center for this function must, consequently, also lie outside of the spinal cord. In these experiments, however, the lesion of the spinal cord necessarily produces certain changes of the functions. Extirpation of the lowermost portion of the spinal cord, or simply transverse section, is followed by a complete loss of the influence of the will upon the evacuation of the bladder and rectum, and such evacuation becomes purely automatic, as may easily be recognized from the behavior of the animal. The animals are, of course, anesthetic for the process of evacuation. Immediately after extirpation of the sacral cord the anus gapes from paralysis of the striated sphincter, but it gradually becomes closed, evidently as a result of the vicarious action of the involuntary musculature of the internal sphincter. The striated sphincter, however, remains paralyzed, and the anal reflex (p. 988) is permanently destroyed. If the spinal cord be simply divided above the sacral segment, the tonus of the sphincter and the anal reflex are maintained; in fact, both may even be accentuated. The voluntary perineal muscles which assist in the voluntary closure of the bladder are possibly affected in the same manner as the external sphincter of the anus, although Müller makes no definite statements in this connection. They are paralyzed by destruction of the sacral cord, but the closure of the bladder is effected vicariously by the involuntary sphincter. The experimental results seem to indicate that reflex erection is associated with the maintenance of the lowermost portion of the sacral cord, but that psychic erection is dependent upon the maintenance of the lower dorsal cord. The lower sacral cord consequently seems to receive the sensory fibers from the penis, and to give rise to the genital reflex, while the centrifugal fibers from the brain to the sexual centers evidently leave the spinal cord in the lowermost dorsal segment. Semen may de discharged even after the destruction of the lowermost portion of the spinal

[1] Pflüger's Arch., vol. viii, ix, and lxiii.
[2] Zeit. f. Nervenheilk., vol. xxi, parts 1 and 2.

cord, but a vigorous reflex ejaculation is dependent upon its integrity, *i. e.*, upon the innervation of the voluntary muscles (bulbocavernosus, etc.).

From these experimental data it is easy to assume: (1) That the actual centers for the evacuation of the bladder and rectum, as well as those for erection and ejaculation, are situated outside of the spinal cord in the sympathetic system; (2) that motor fibers reach this sympathetic apparatus through the spinal cord by means of the rami communicantes, from the lumbar and sacral segments; and (3) that the motor fibers for the striated muscles of the pelvic floor, which effect the voluntary closure of the bladder and rectum, and aid during ejaculation, also the motor fibers to the muscles concerned in abdominal straining, arise directly from the spinal cord, and have nothing to do with the sympathetic. The sensory impulses for the reflex innervation of these muscles and to the brain are necessarily conducted by the spinal cord. According to this conception, the only part played by the spinal cord in the vesical and rectal functions and the genital reflex is the conduction of sensory impulses to the brain and of voluntary cerebral impulses for the innervation and

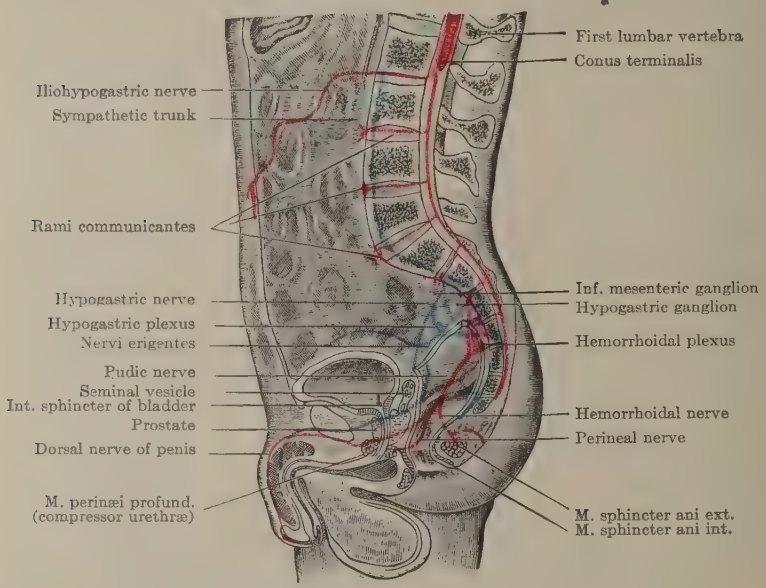


Fig. 471.—Diagram of the rectal and vesical innervation (according to Müller).

relaxation of the striated vesical and rectal sphincters, for the innervation of the muscles concerned in abdominal straining, and for the reflex influence upon these voluntary muscles. The actual bladder and rectal reflexes may be accomplished autonomously by the sympathetic, without the aid of the spinal cord.

Supported by his own investigations, as well as by those of Rehfisch,[1] Müller completely repudiates the old theory of the spinal centers for the bladder, rectum, and ejaculation, and constructs the diagram shown in Fig. 471 for the explanation of the clinical symptoms in patients with affections of the spinal cord, in which only the sympathetic plexus is to be regarded as a central mechanism.

According to this new theory, the clinical symptoms in the human subject are easily explained if we assume, with Müller, that in all destructive lesions of the spinal cord, whether they involve the sacral, the lumbar, or higher regions, the primary disturbance is always urinary and fecal retention, followed by paradoxic incontinence, that typical periodic evacuations are always established later, and

[1] Virchow's Archiv, vol. clxi.

that permanent disturbances in affections of the spinal cord, like the initial retention and paradoxic incontinence, are due simply to the absence of sensation as well as of the voluntary components of evacuation. Further investigations are necessary, however, to determine whether these suppositions are really in accord with clinical observations. The peculiar vesical disturbances in tabes dorsalis are certainly easy of explanation by Müller's theory, even without assuming, as does Müller, that in these cases the tabes is localized in the sympathetic. Also according to Müller's theory the sensory disturbances in tabes are sufficient to explain both the retention and the slight phenomena of incontinence in these patients, since the regulating influence of the spinal cord and brain is more or less impaired as a result of the disturbed vesical sensibility. The sexual disturbances in patients with affections of the spinal cord may also be easily explained by Müller's diagram if we remember that the lesion hinders the transmission of the psychic excitations from the lower dorsal cord to the sympathetic sexual center, and that variations of the reflex irritability of the lowermost portions of the cord in spinal lesions may increase or diminish the reflex components of erection or ejaculation. (See above.) The fact that patients with destruction of the sacral cord and complete motor and sensory paralysis of the lower half of the body are still capable of procreation (examples of which are given by Müller) is best explained by the new theory.

It must be said that Müller's theory contains much that is plausible in reference to the non-striated musculature of the bladder and rectum, the spinal innervation of which, according to the old theory, always seemed rather dubious. His experiments also seem to be quite convincing, but the author, nevertheless, believes that they are not entirely free from objection. For instance, these experiments, as well as those of Goltz and Ewald, have not certainly demonstrated that the vesical and rectal functions are carried on with the same vigor and precision after the destruction of the spinal cord as they were before, that the strength of the involuntary sphincters and detrusors does not also suffer, and that the degree of distention of the bladder and rectum prior to evacuation is the same without the influence of the spinal cord as it is with it. If we assume, according to the old theory (p. 1166 et seq.), that the reflex mechanism of the bladder and of the rectum consists of a number of superimposed reflex arcs, it becomes quite plausible to conclude that the lowermost of these arcs is situated in the sympathetic, and that it is associated with spinal, and even cerebral, reflex arcs in such a manner that in case of necessity the sympathetic arc may carry on these functions, but that the finer and more vigorous functions are possible only with the coöperation of the spinal cord and brain. It is possibly a verbal quibble whether we regard the functions of the sympathetic, of the cord, and of the brain as occurring in reflex arcs, or whether we assume that the reflex function belongs only to the sympathetic, and that the higher functions of the cord and brain are excluded from this reflex. Since every nervous function proceeds upon the principle of a reflex, however, the former supposition seems to be fully justified, and, as a matter of fact, Müller admits the importance of the spinal elements of the reflex concerned in a powerful ejaculation. (See above.) In this way the superimposed spinal reflex arcs communicating with the sympathetic would act as supplementary relays in emptying the bladder and rectum. Moreover, there is really no reason to contest the qualification of bladder and rectal centers for those reflex centers which the striated sphincters of these structures (loss of tonus of the sphincter after destruction of the cord—Müller) and, in fact, every voluntary muscle, must possess in the cord. By the conception of superimposed reflex arcs, however, it seems to the author that the two theories may be made to harmonize. The recorded experiments are not sufficient to decide this question. The preservation of the vesical and rectal functions after destruction of the cord has not as yet been sufficiently explained by experiments, and it must be studied both quantitatively and qualitatively more carefully than has been done either clinically or experimentally.

Examining the Vesical and Rectal Functions

In examining the disturbed bladder and rectal functions the following points should be noted:

1. Fulness of the bladder and of the rectum—to be determined by palpation and percussion in the case of the bladder, and by digital examination in the case of the rectum.

2. Condition of the sphincter tonus—to be determined for the bladder by attempting to expel its contents mechanically or with the help of the catheter; for the rectum, by digital examination.

3. Sensibility of the bladder and rectal mucous membranes.[1] The occurrence or lack of a desire for stool or urination will decide this point. The sensibility of the bladder can also be determined by a catheter; the rectum by a digital examination. Pain or pressure (tenesmus) accompanying evacuation should be heeded.

4. Character of the evacuation: Absolute or partial retention of the urine and feces; overflow of the full bladder and the rectum, with pronounced retention and accentuated sphincter tonus (the real *paradoxic incontinence*). Degree of retention: palpatory determination of the position of the fundus of the bladder; involuntary evacuation by means of the normal reflexes (*enuresis, involuntary defecation*); possibility or impossibility of favoring the reflex involuntary evacuation (incontinence) or of inhibiting it. *Imperative incontinence* is the name applied to a special form of incontinence in which the only way to avoid an involuntary escape of urine or feces is immediately to accede to the very first demand for evacuation. The fact that constipation often occurs without any spinal cord affection makes it difficult to determine practically how much clinical value is to be assigned to the condition of the rectal evacuation. Therefore, before deciding that a constipation depends upon the spinal cord, it is especially important to examine points 1, 2, and 3. In any analysis of the character of evacuation we must also determine whether or not the patient still preserves the sensation of micturition and defecation, being careful to avoid confusing this sensation with that of being wet or soiled.

APPENDIX

The Utility of Routine Plans and Stamped or Printed Figures for Collecting and Tabulating the Results of Examination

ROUTINE PLANS

In tabulating the condition of a patient for certain special purposes it has been found very advantageous at the author's clinic to make use of definite routine plans. In this way nothing important in the examination can be forgotten, and the results will be entered in a careful and summarized fashion. These outlines have proved of so much value, and saved so much time, that it seems worth while to give examples of them.

They are of special value in examining the nervous system, both because the points upon which the complete examination depends are almost too numerous to keep constantly in mind, and because it is especially advantageous in this class of diseases to group the results of examination in an intelligent way. (See p. 946.) Of course, they are also valuable in examining other affections. A few examples will illustrate this, although it scarcely need be mentioned that the outlines may be modified or enlarged at pleasure, according to the special purpose of the examiner. The following examples should in no way be considered as absolute standards, but merely as illustrations of what the author has found useful. Enough space upon the right side of the text should be reserved to enter the necessary notes. For the nervous system it is advisable to leave sufficient space for the data upon both sides, to correspond to the right and left sides of the body. Everything found to be "normal" should be marked so, and everything which has not been examined should be marked "not examined." Naturally, the entire status cannot be settled in every instance by filling out the outlines, because some conditions often require a more detailed description; but the outlines will serve to a certain extent as a nucleus for the entire clinical picture, about which everything else crystallizes. To prevent misunderstanding, the author wishes to call attention to the fact that such outlines do not in any way take the place of the ordinary extended descriptions of the symptoms of disease. Experience shows it to be entirely impractical to use them, except for certain special examinations.

[1] It has not been determined how much actual sensibility the mucous membranes of the bladder and rectum normally possess; nor to what extent the consciousness of a full bladder or rectum is caused by stretching of its nearby soft parts innervated by the spinal nerves. It is possible that, under normal conditions, just as in the case of the intestines, gall-bladder, etc., only the stimuli from the soft parts reach the brain, and that the vesical mucous membrane becomes sensitive only when diseased. (See p. 981.)

1. OUTLINE FOR THE EXAMINATION OF THE DIGESTION

Name.
Date.
Appetite. Stool. Vomiting (time, character).
Retention in the morning. Pains (time, character).

Characteristics of the Gastric Contents:[1]

The Vomitus: Mucus, blood, leukocytes, meat-fibers, starch, sarcinæ, bacteria.
The Expressed Contents of the Empty Stomach: Mucus, blood, leukocytes, meat-fibers, starch, residue of other food, sarcinæ, bacteria.
The expressed contents of the empty stomach after the withdrawal of the gastric contents on the preceding evening.

Butyrometric Gastric Examination:

Amount of test-meal prepared . . cc., containing . . gm. flour and . . gm. butter.
Amount of test-meal ingested . . cc.
Expression after . . minutes. Amount expressed (by method of complete evacuation of stomach, p. 444): . . cc.
Acidity of the filtrate of the expressed meal: a . . cc. $\frac{N}{10}$ NaOH to 10 cc. contents = % HCl.

Free HCl $\begin{cases} = + \text{ . . \% HCl (acid excess).} \\ = - \text{ . . \% HCl (acid deficit).} \end{cases}$

Lactic acid: [Shaking with ether].
Fat percentage of the ingested flour soup (estimated butyrometrically): F = . . %.
Fat percentage of the expressed flour soup (estimated butyrometrically): f = . . %.
Residual amount of meal: $Su = \frac{f}{F}\,To$ = . . cc. (because $\frac{Su}{To} = \frac{f}{F}$).
Amount of gastric juice: $Ma = To - Su$ = . . cc.
Acidity of the pure secretion: $A = \frac{a\,To}{Ma}$ = . . % (because $\frac{a}{A} = \frac{Ma}{To}$).
Secretion quotient: $\frac{Ma}{Su}$ =
Motility quotient: $\frac{\text{the soup which passes through the intestine}}{\text{soup ingested}}$ =
Summary of results: $\overbrace{Su = \qquad\qquad Ma =}^{To}\ A =$

Examination of the Filtrate of the Gastric Contents

(*a*) *Of the Flour Soup Breakfast:*
Reaction to free HCl: . . . Phloroglucinvanillin . . . Methyl-violet . . . Tropaolin . . .
Rennin ferment.
Starch digestion: Coloration of 5 cc. of the gastric juice filtrate after addition of . . cc. of $\frac{N}{100}$ iodid solution.
This color is blue,[1] violet,[1] red.[1]
Test of digestion with carmin fibrin:
1. With unmixed gastric juice.
2. With undiluted or acidified gastric juice.

(*b*) Of the vomitus . . . hours after ingestion of food.
Same with the test-breakfast.

The Desmoid Reaction

The desmoid capsule taken at noon after soup. The patient ambulant or in bed (lying, sitting) avoiding right lateral posture. (See p. 433.)
Appearance of methylene-blue in urine after . . . hours.
Negative after . . . . hours.

[1] What is not found should be crossed out.

Iodoform Glutoid Test

Control number of the capsules . .
Appearance of the first iodid reaction in the saliva after . . hours.
Duration of the reaction.
Results on a healthy individual.

2. OUTLINE FOR THE EXAMINATION OF CASES OF DIPHTHERIA AND OTHER ANGINAS[1]

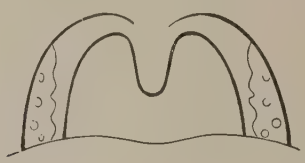


Fig. 472.—Diagram to represent the localization of the membrane.

Name.
Age.
Date.
day of illness.
Hoarseness.
Stenotic phenomena.
Membrane. No visible membrane. nasal cavity. buccal cavity. tonsils. pillars of fauces. soft palate. posterior pharyngeal wall. larynx. trachea other locations.

Kind of membrane in the throat or vicinity.	Punctiform.	Tenacious.	Thick.	Firmly adherent.	Grayish.
	Patchy.	Soft.	Thin.	Easily wiped off.	Yellowish.
	Continuous.		Flimsy.		

Parts surrounding the membranes: Very red swollen little changed.
Lymph-glands: not little much swollen.
Angina lacunaris (punctiform membrane projecting from the depth of the crypts).
Angina catarrhalis.
Results of lung examination.
Albuminuria.
Bacteriologic findings.
Dry preparation (from where?).
Culture (from where?). Upon what medium?
Further notes.

3. OUTLINE FOR THE EXAMINATION OF THE BLOOD

Name.
Date.
Hemoglobin.
Number of erythrocytes.
Quotient (hemoglobin value of the individual erythrocyte).
Volume quotient of erythrocytes.
Number of leukocytes.

Morphologic Examination

(*a*) *Fresh Specimen.*
Formation of rouleaux.
Fibrin.
Blood-platelets.
Poikilocytosis.
(*b*) *Stained and Fixed Specimen.*
Staining method.
Erythrocytes.
Shape.
Size.

[1] What is not found should be crossed out.

Tinctorial peculiarities (diminished hemoglobin, polychromasia, basophilic granulation).
Nucleated reds. Normoblasts. Megaloblasts.
Differentiation of the leukocytes. (How many counted?).
Per cent. of the total number. Absolute number per c.mm.

- Polymorphonuclear
  - Neutrophilic.
  - Eosinophilic.
  - Mast cells.
- Mononuclear
  - Large mononuclear without granulations.
  - Transition forms.
  - Lymphocytes
    - Normal.
    - Abnormal.
  - Myelocytes
    - Neutrophilic.
    - Eosinophilic.
    - Mast cells.

Unusual forms.
Malarial parasites, bacteria.
Other observations.
(If there was an autopsy) condition of bone-marrow.

4. OUTLINE FOR THE EXAMINATION OF THE NERVOUS SYSTEM

(a) General Outline

Date.
Name.
Sensorium.
Intelligence.
Disposition.
Memory.
Sleep, vertigo.
Speech. (For details, see special scheme, p. 1122.)
Breathing.
Pulse.
Cranial nerves. (For details, see special scheme *b*, p. 1175.)
Attitude.
Gait (with eyes open and shut).
Standing position (with eyes open and shut).

Voluntary Motility

Neck:
- Sternocleidomastoid.
- Trapezius.
- Other muscles of the neck.

Upper extremity. (For details, see special scheme, p. 1132.)
- Gross muscular power.
- Coördination.

Lower extremity. (For details, see special scheme, p. 1134.)
- Gross muscular power.
- Coördination.

Trunk:
- Intercostal muscles.
- Diaphragm.
- Abdominal muscles.
- Muscles of the back.

Irritative motor phenomena (clonic, tonic spasms, fibrillary twitchings, tremors, contractures, chorea, athetosis, etc.).
Muscular atrophies:
Electric reaction of the muscles. (For details, see special scheme *d*, p. 1176.)

Sensibility

(To be represented upon a chart of the body.[1] It should be mentioned here how the sensations of touch, pain, heat, cold, and pressure, etc. were examined.)

[1] See p. 1177.

Head and Neck:
- Sensation of touch.
- Bony and cutaneous perception of vibrations.
- Sensation of pain.
- Sensation of heat.
- Sensation of cold.
- Localization of pain and touch.

Upper Extremity:
- Sensation of touch.
- Bony and cutaneous perception of vibrations.
- Sensation of pain.
- Sensation of heat.
- Sensation of cold.
- Sensation of pressure.
- Localization of pain and touch.
- Innervation sense, "power sense."
- Appreciation and judgment of the active movements.
- Appreciation of posture.[1]
- Appreciation of an object by feeling it (stereognostic sense).

Trunk:
- Sensation of touch.
- Bony and cutaneous perception of vibrations.
- Sensation of pain.
- Sensation of heat.
- Sensation of cold.
- Sensation of pressure.
- Localization of pain and touch.

Lower Extremity:
- Sensation of touch.
- Bony and cutaneous perception of vibrations.
- Sensation of pain.
- Sensation of heat.
- Sensation of cold.
- Sensation of pressure.
- Localization of pain and touch.
- Innervation sense, "power sense."
- Appreciation and judgment of the active movements.
- Appreciation of posture.[2]
- Appreciation of an object by feeling it (stereognostic sense).

Spontaneous pains (neuralgias, parenchymatous pains, headache).
Hyperalgesia of the skin.
Sensibility of the nerves and muscles to pressure.

Reflexes

Cutaneous Reflexes (strength? alteration?).[3]
- Plantar reflex (to pricking).
- Plantar reflex (to tickling).
- Abdominal reflex (upper, lower, middle).
- Cremaster reflex (groin reflex).
- Anal reflex.
- Other reflexes.

Tendon Reflexes.
- Patellar reflex.
- Achilles reflex (foot clonus).
- Upper extremity.

Periosteal reflexes.

Bladder Functions

Fulness of the bladder.

Condition of the sphincter tonus (expression of the bladder, finally examining with a catheter.)

Sensibility of the bladder mucous membrane. Desire for evacuation, urgency, tenesmus, pains.

Character of the evacuation: Absolute or partial retention; overflow of a full bladder associated with a marked retention and an increased sphincter tonus (*paradoxic*

[1] See p. 978 et seq. [2] See p. 976 et seq. [3] See p. 997, Pathologic Reflexes.

incontinence); degree of retention; overflow of the bladder with a moderate filling and deficient sphincter tonus (*actual paralysis of the bladder*); the position of the fundus (palpation); evacuation through the normal reflex, but involuntarily (*enuresis*); possibility or impossibility of influencing the reflex evacuation, either favoring (incontinence, imperative incontinence, p. 1170) or inhibiting it. Sensation produced by the evacuation to be distinguished from the sensation of the wetting.

FUNCTIONS OF THE RECTUM

Character of the stool evacuation. For the rest, we employ practically the same scheme as for the bladder functions.

Condition of the nervous sexual apparatus. (Potency, etc.)

Trophic disturbances of the skin, hair, nails, decubitus, ulcus perforans, etc.

Vasomotor conditions.

Additional notes.

(*b*) Outline for the Examination of the Cranial Nerves

Date.
Name.

I. *Olfactory.*
- Smell (how tested? cologne water, asafetida, ol. anisi).
- Result of rhinoscopic examination.

II. *Optic.*
- Central visual acuity (with corrected refraction).
- Visual field (hemiopia, limitations, fatigue).
- Result of ophthalmoscopic examination.
- Color blindness (how examined? Holmgren-Pflüger's flower contrast).

III, IV, VI. *Nerves of the Eye Muscles.*
- Direction of vision (conjugate deviation).
- Conjugate movements.
- Unilateral testing of the movements of the eyes.
- Double vision.
- Convergence (how tested?).
- Nystagmus:
  - Horizontal.
  - Vertical.
  - Rotatory.
- Pupils:
  - Size under moderate illumination.
  - Reaction to light (how tested?).
    - Direct.
    - Crossed.
  - Hemiopic rigidity to light (to be tested in hemiopia and double blindness, how tested?).
  - Reaction to accommodation.
- Accommodation (how tested?).

V. *Trigeminus.*
- Sensory division.
  - Face.
  - Forehead.
  - Conjunctiva and cornea (corneal reflex).
  - Tongue.
  - Taste (how tested? salt, acetic acid).
  - Smell (how tested? acetic acid, ammonia).
- Motor division (chewing muscles).
  - Raising the jaw.
  - Lateral movement of the jaw.
  - Atrophy of the chewing muscles.
  - Electric examination. (See special scheme.)

VII. *Facial.*
- Upper branch (forehead, closure of eyes).
- Lower branch.
- Palate (position, voluntary movement, speech, swallowing, reflex).
- Electric examination. (For details, see special scheme.)
- Behavior of the facial associated movements.

VII. *Facial (Continued).*
- Behavior of the facial emotional movements.
- Corneal reflex, optic facial reflex.
- Mechanical irritability (how tested?).
- Atrophy of the facial muscles.

VIII. *Acoustic.*
- Hearing in general.
- Test of the air conduction.
- Test of the bone conduction (von Bezold's modification of Rinne's test).
  - Weber's test.
  - Schwabach's test.
- Subjective noises, dizziness.
- Results of otoscopic examination.

IX, X, XI. *Glossopharyngeal, Vagus, Accessory.*
- Taste (how tested? bitter, sweet?).
- Act of swallowing.
- Voice.
- Breathing and pulse.
- Results of laryngoscopic examination.
- Trapezius, sternocleidomastoideus.
- Atrophies.
- Electric examination. (For details, see special scheme.)

XII. *Hypoglossal.*
- Extended movements.
- Position of the tongue when protruded.
- Atrophy of the tongue.
- Fibrillary twitching.
- Electric examination. (For details, see special scheme.)
- Speech. (See special scheme.)

Other Remarks.

(*c*) Outlines for the Examination of Muscular Atrophies and Peripheral Motor Paralyses

For the exact examination of the motility of the individual muscles and the peripheral motor nerves, the Bern Clinic uses the outline found upon pp. 1132–1136. Ample room should be left for the entries, and the outlines for the upper and the lower extremity should be printed upon separate sheets.

(*d*) Outlines for Electric Examination

Corresponding results of examining a healthy individual of equal stature and constitution, for comparison.

Date.
Name.
Name of the muscle examined.
Size in sq. c. of the stimulation electrode employed.

Examination of the Muscle

Faradic Current.
- Rapid interruption. Minimum contraction measured upon the sliding apparatus. Type of contraction.
- Single shocks. Minimum contraction measured upon the sliding apparatus. Type of contraction.
- Signs of fatigue.

Galvanic Current.
- Minimal CaCC in milliampères. Volt.
  - Type of contraction.
- Minimal AnCC in milliampères. Volt.
  - Type of contraction.
- Relation of CaCC to AnCC in milliampères. Volt.
- Signs of fatigue.

Examination of the Nerve

Point of Stimulation:
Faradic Current.
- Rapid interruption. Minimal contraction measured upon the sliding apparatus. Type of contraction.

Faradic Current (Continued).
Single shocks. Minimal contraction measured upon the sliding apparatus.
Type of contraction.
Signs of fatigue.
Galvanic Current.
Minimal CaCC in milliampères. Volt.
Type of contraction.
Minimal AnCC in milliampères. Volt.
Type of contraction.
Relation of CaCC to AnCC in milliampères. Volt.
Signs of fatigue.

Especial Types of Reactions.
Myotonic reaction, galvanic myokymia, faradic myokymia, neurotonic reaction, myasthenic reaction, alternating contractions during faradic stimulation, myotonomia during faradic stimulation, etc.

(e) Outline for the Examination of the Speech

The summary upon p. 1122 may be utilized as an outline.

CHARTS

Charts are especially useful for recording the results of physical examinations. The fundamental rules recommended for their use are mentioned upon pp. 209 et seq., 217 et seq., 310, 327, 334 to 339, 345, and condensed upon pp. 388 and 408 et seq. They are employed in all the histories in Bern. Upon pp. 223 to 272 and 388 to 421 a large number of examples of pathologic charts are to be found. The charts on pp. 209 to 211—better double the size—are good models. Exact representations are difficult to make upon the ordinary small chart. For routine office practice, however, rubber stamps are very serviceable. In the author's experience the use of pictorial charts, especially, for the designation of pulmonary and cardiac lesions, cannot be too highly recommended. They compel a more thorough examination, in the same way that one who makes sketches during a journey necessarily observes objects more accurately than one who does not. A few strokes of the pencil often mean more to the traveler or diagnostician than a lengthy description.

Charts are quite as essential for representing disturbances of sensibility. The linear reproductions on pp. 1136 to 1141, Figs. 449 to 454, may be used as charts representing circumscribed disturbances of sensibility. Those upon pp. 948 and 985 are better for representing disturbances which affect a large part of the entire body (hemiplegias, paraplegias, hysteric disturbances of sensibility). The variations of sensibility can be best expressed upon these charts by different colors or shading.

Charts are also useful for representing laryngoscopic, rhinoscopic, and otoscopic lesions (Fig. 339, p. 900, and Fig. 357. p. 906).

The results of ophthalmoscopic examination may be very conveniently represented graphically in the sketch-book prepared by Prof. Haab (sold by Hofer Burger, in Zurich). Both plates in this book have been made by means of this sketch-book. The leaves are colored to represent the red ground-tone of the ophthalmoscopic picture. White or yellow shades can be produced by rubbing this ground-color more or less vigorously with an eraser or a knife, and the dark-red and black tones can be added with colored pencils or water-colors. The technic is explicitly described in the sketch-book, and any one can easily acquire facility enough to make very useful pictures.

[NOTE ON THE CAMMIDGE REACTION (p. 596).

Roper and Stillman,[1] after a careful study of the Cammidge reaction, reach the following conclusions: "The 'C reaction,' as proposed by Cammidge, for the demonstration of a characteristic substance in the urine of patients suffering from diseases of the pancreas, does not rest on a firm scientific basis, as all the glycuronic acid is not removed in every instance by the technic of this reaction. The formation of the typical crystals is due to the presence of glycuronic acid. As this substance is present in the urine of persons in normal health, and is increased in amount in many conditions in no way associated with disease of the pancreas, the demonstration of these so-called typical crystals can have no diagnostic value."—Ed.]

[1] Personal communication.

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